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THE MAJOR FORMS OF HEREDITARY ECTODERMAL DYSPLASIA*

(WITH AN AUTOPSY AND BIOPSIES ON THE ANHYDROTIC TYPE)

BY H. R. CLOUSTON, B.A., M.D., C.M., F.R.C.P.(C.)

Huntingdon, Que.

MY nearest neighbour country general practitioner to the southwest has recently written a book in which he reminds us that there are no illegitimate children; only illegitimate parents. Similarly, it seems that the rare things in medicine are not rare; only observers are rare.

There are two forms of dysplasia confined to ectodermal tissues, and which descend according to Mendelian laws. Both are said to be most uncommon. One type I have recognized and observed for over forty years, and I have had correspondence about cases from Boston to Seattle and from Winnipeg to St. Louis. It is so well marked that my children recognize it on the street, and it is so common that I have seen over 50 cases and know where there are a couple of hundred more. The other type is said to be so rare that it appears that less than three dozen cases have been reported in the whole world; but as soon as it was suggested cases began to show up in Montreal. When fully developed one type perspires freely and the other does not; so they have been called the hydrotic and the anhydrotic types, respectively.

The earliest growth of the fertilized egg results in three layers. From the outer layer or ectoderm we get the outer skin, the hair, nails, sweat and sebaceous glands, tooth enamel, the lining of the nose and mouth and certain other openings, the nervous system, the adrenal medulla and the pituitary body.

The hydrotic type acts as a Mendelian dominant, not sex-linked. Males and females are affected equally, males and females transmit it equally, and one-half of the children of the defectives show the defect. It never skips a generation. If a child has the defect either his father or his mother had it before him. All the subjects are hybrids. Two of them have never married and therefore it has never been seen in the human subject except in the heterozygous state. Experiments with this type in mice would indicate that the condition is lethal or sublethal in the homozygous state. There are probably several thousand of these people in America, but it seems clear that all have descended from one individual who lived in France more than 200 years ago, and that the whole group is the result of a single mutation.

The affection always shows in the nails, which are short, thick, and slowly growing. In extreme cases there are no nails at all on either hand or foot. It is important to note that all grades of the dysplasia can be found. With this nail defect there is almost always some hair defect. Some subjects have no hair of any kind anywhere, and those who have it complain that it does not wear well. It has not the normal resistance to rubbing by hat bands, etc. It breaks off close to the skin where there is much friction. This is probably due to imperfect keratinization. The skin of the palms of the hands frequently appears rough and thickened, is of poor quality and cracks readily. We have been calling this condition a hyperkeratosis but in reality it is a dyskeratosis. In general, cancer of the working surface of the hand is quite uncommon, but two of these people developed it there. One was a washerwoman and the other a carpenter. Another subject had a cancer of the tongue.

Skin pigmentation is marked and is peculiar enough that those who live among the cases

* Adapted from a paper read at the Sixty-ninth Annual Meeting of the Canadian Medical Association, Section of Medicine, Halifax, June 24, 1938.

can often recognize it on the street by the colour alone. It affects certain parts more particularly, the knuckles, elbows, axillæ, nipple areola, pubes, and the ischial tuberosities, etc. One boy had a deep pigmentation of the umbilicus and the linea alba such as is seen in pregnancy. Naturally it was a false alarm! Blood pressures are usually low and such people may live to good old ages. These low blood pressures and pigmentations suggest Addison's disease. The adrenals are under the control of the ectodermal anterior pituitary body, and the medulla itself is ectodermal.

At one time it was thought that the whole condition was due to hypothyroidism, but it is easily shown that this is not so. Low basal metabolic rates however are so constant that they require explanation.

The pituitary body is derived from the ectoderm, the anterior portion very directly, and certain of the functions deviate to the right or left of normal. These will be discussed in conjunction with the findings in the anhydrotic type. David[1] did reciprocal transplants of skin between the normal and defective mice. The normal skin remained normal on the defective mouse and the defective skin remained defective on the normal mouse. Again, normal mice and defective mice were placed into a parabiotic union (*i.e.*, artificial Siamese twins). Neither skin was affected by the serum of the other mouse. These two experiments seem to show conclusively that the cause is not endocrine.

There are many neurological defects in the group, *e.g.*, stammering. The number of mental defectives is abnormally large.

Eye troubles are common. Part of these, such as conjunctivitis and pterygium, are probably due to mechanical causes such as absence of the lashes. Another part is inherent. Strabismus is common, and I have seen one case of double congenital cataract. The lashes, the lens, and the conjunctiva are all ectodermal.

From a study of 40 cases in four generations I have compiled a chart which confirms the belief of the families that the average condition has decreased in intensity from generation to generation. I feel sure that I have seen improvement in the individual case through improved living conditions, and am equally certain that the same thing occurs in families. The statisticians point out, however, that the figures are not sufficient to establish with certainty that there is a definite trend which will continue (see Chart 1).

The condition is quite definitely not luetic, but syphilis does occur. (For a more extended description with illustrations and charts see my previous article in this *Journal*[2]).

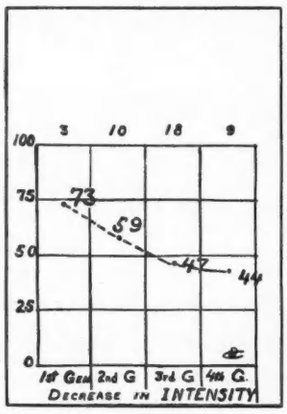

Chart 1

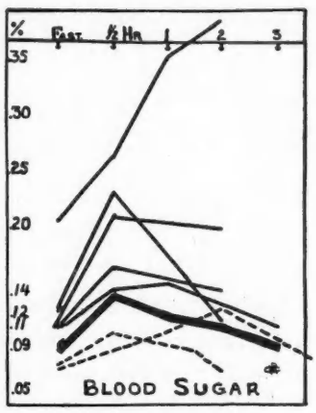

Chart 2

Chart 2.—Heavy line is Joslin's average normal. Narrow lines are curves of the hydrotic type. Broken lines are curves of the anhydrotic cases.

THE ANHYDROTIC TYPE

Only about 30 cases have been described. The defect is a recessive, and there is rarely a history of it in the family. Two of our patients were brothers. (In two or three instances it has appeared, possibly, as a dominant, but the evidence has not been completely satisfactory). Practically all the cases are in males, and it is generally stated that the condition is sex-linked, but certain cases have been reported in the female, and in mice both sexes are affected. Our four cases are in males. The distinctive marks of the condition are: (1) Diminished sweating; sweat glands are absent even up to 100 per cent. (2) Dental aplasia—missing teeth and deformed teeth and the teeth may be entirely absent. (3) A rhinitis which has usually been called "atrophic" but which is really a "hypoplastic rhinitis". Our autopsy showed almost a complete absence of the mucous glands of the nose and throat. (4) Some abnormality of the hair.

Cases have been reported from India, Russia, Germany, Sweden, France, England, among the Jews, United States of America, and from Australia. Our cases are from French and English Canada.

This world-wide distribution means one of two things, *viz.*, either the original mutation occurred a very long time ago, or, more likely, it is a mutation which occurs very readily and has

done so a number of times. In either event it is obvious that three dozen cases do not begin to represent the true number of them. There must be hundreds. Unlike the hydrotic type there is no apparent impediment to marriage in the heterozygous state. On the other hand it is absurd to suppose that the clinicians of the world would miss a condition which is so distinctive when it is fully developed. In the hydrotic type I can show every grade of the defect, and all the evidence points to the fact that there is every degree of severity in the anhydrotic cases also. The evident discrepancy between the theoretical and the observed incidence is probably explained by unrecognized cases which fall into three groups.

First, there is a large group of severe cases with almost complete lack of sweat glands, which therefore have no emergency temperature control. Hyperpyrexia occurs on the slightest excuse. Two of our infants suddenly showed temperatures of 108° F., apparently due to being too heavily covered in hot weather. Also, as we are able to show by autopsy for the first time, there may be lack of the mucous glands of the nose and throat. The accepted teaching is that the nasal mucosa warms the air, moistens it and washes it relatively free from germs before entering the lungs. It is the first line of defence of the body. The ultra-modern air-conditioning systems of our day really had their prototype in the nose and throat of our ultimate great grandfather Adam (see Figs. 4a and 5a).

Lacking this defensive apparatus and lacking temperature control, these infants probably die off with rhinitis, otitis media, pneumonia, and hyperpyrexia with or without convulsions. They die before the distinctive dentition has occurred and before they are old enough to complain of the heat, and the true condition is not suspected. Two of our cases would have fallen into this group. We have here a previously unrecognized cause of death in infancy.

The second group probably consists of those passed over as congenital syphilis. Our profession has been prone to consider any abnormal skin and tooth condition as luetic. One of our patients, aged 3, would have been so classified.

It seems probable, according to my theory, that the third group is made up of those cases which are relatively mild. No one asks whether a drop of sweat is produced by one gland working actively or two at half speed. The grown-ups have dentures and in the case of children the clinician supposes that the teeth have fallen out, or that there is delayed eruption. The chief complaint of our fourth patient was ozæna. The other factors were present but were made endurable.

In the average cases reported the absence of sweating makes life miserable. Hot weather, hot rooms, hot drinks, or heavy clothes cause elevations in temperature and suffering. One of these patients, who was working in the hay field, hired a boy to fetch water from a brook and throw it over him. Another capitalized his misfortune by becoming a life-guard at a beach. All grown subjects have learned to carry a wet cloth with which to moisten themselves, in order to control the temperature by evaporation.

Through the courtesy of the Children's Memorial Hospital and the Royal Victoria Hospital, of Montreal, I am able to report three of their cases. The fourth case was seen privately.

THE TEETH

Patient 1.—Age 4 months. No buds were visible by x-ray. Microscopic examination at autopsy showed no tooth foci.

Patient 2.—Age 6 months (brother of patient 1). None erupted; x-ray shows only three buds in the lower jaw and many missing in the upper jaw.

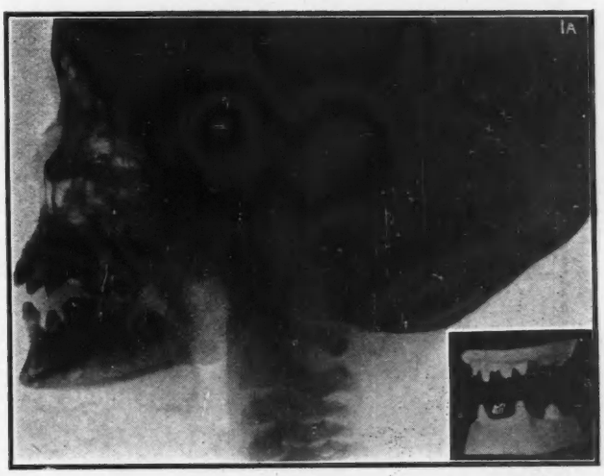

Fig. 1a (Patient 4).—Note sparseness of teeth and buds. **Fig. 1b.**—Plaster cast of teeth.

Patient 3.—Only two teeth were erupted at 3 years. X-ray shows four teeth in the upper jaw and only one bud in the lower jaw. This is possibly a canine.

Patient 4.—At seven years has 12 teeth erupted. The four upper molars and two lower molars are fairly normal. Anteriorly there are four uppers and two lowers. These cannot be identified by shape as they taper from a round base to a point. This is the primitive form of teeth. The lowers occupy the position of cuspids and are very literally canine in shape. The points were so long and so sharp that they had to be ground off by the dentist, because of injury to the opposing jaw. (In mice this may become a cause of death). X-ray shows only 6 unerupted buds, and he has lost no teeth. This makes a total of 18 against a normal of 52 (Figs. 1a and 1b).

THE SKIN

Patient 1.—At birth the nurse notified the mother that the child had some skin disease and prognosticated trouble in this respect.

Patient 2.—He was breast-fed for 6 weeks, but this was stopped because the baby would develop a rash on the side of the face that was against the mother during nursing. The skin was always dry, and the child resented being heavily clothed and cried when dressed to be taken out of doors. The skin was very dry and there was a tendency to desquamation.

Patient 3.—The skin was dry, shiny, with almost complete lack of hair.

Patient 4.—At birth was covered by a sort of scum which was two weeks or more in disappearing. "Eczema" all over the body gave a great deal of trouble for two years or more. The ears cracked and so did the elbows.

THE SWEAT GLANDS

Patient 1.—Skin sections for microscopic examination were taken from the axilla, anterior and lateral chest wall, from the back, abdomen, pubic region and the scalp. No definite sweat gland cells were found in any section.

Patient 2.—Sections were taken from the breast, (Fig. 3a), axilla, left lumbar, sole of foot and posterior aspect of the scrotum. No sweat glands were found in any area.

Patient 3.—The section was from the mid-line in the back, the thoracic region. No sweat glands were found.

Patient 4.—Sweats visibly, but less than others in the family.

Attempts had been made to cause sweating in patients 2 and 3 by the use of pilocarpine. For obvious reasons these were futile. First discovered by accident and later confirmed by design, patients 1, 2 and 3 showed rapid elevation of temperature if unduly covered or surrounded by heat.

THE SEBACEOUS GLANDS

Patient 1.—A few sebaceous glands were found in the skin taken from the back, but were absent or rudimentary in all the other areas examined (Fig. 2a shows a section from the pubic region).

Patient 2.—No trace of sebaceous glands was found, even on the posterior aspect of the scrotum.

Patient 3.—One normal sebaceous gland was found. However, there are fairly numerous masses budding off from the hair follicles which appear to be immature sebaceous glands.

Patient 4.—No biopsy.

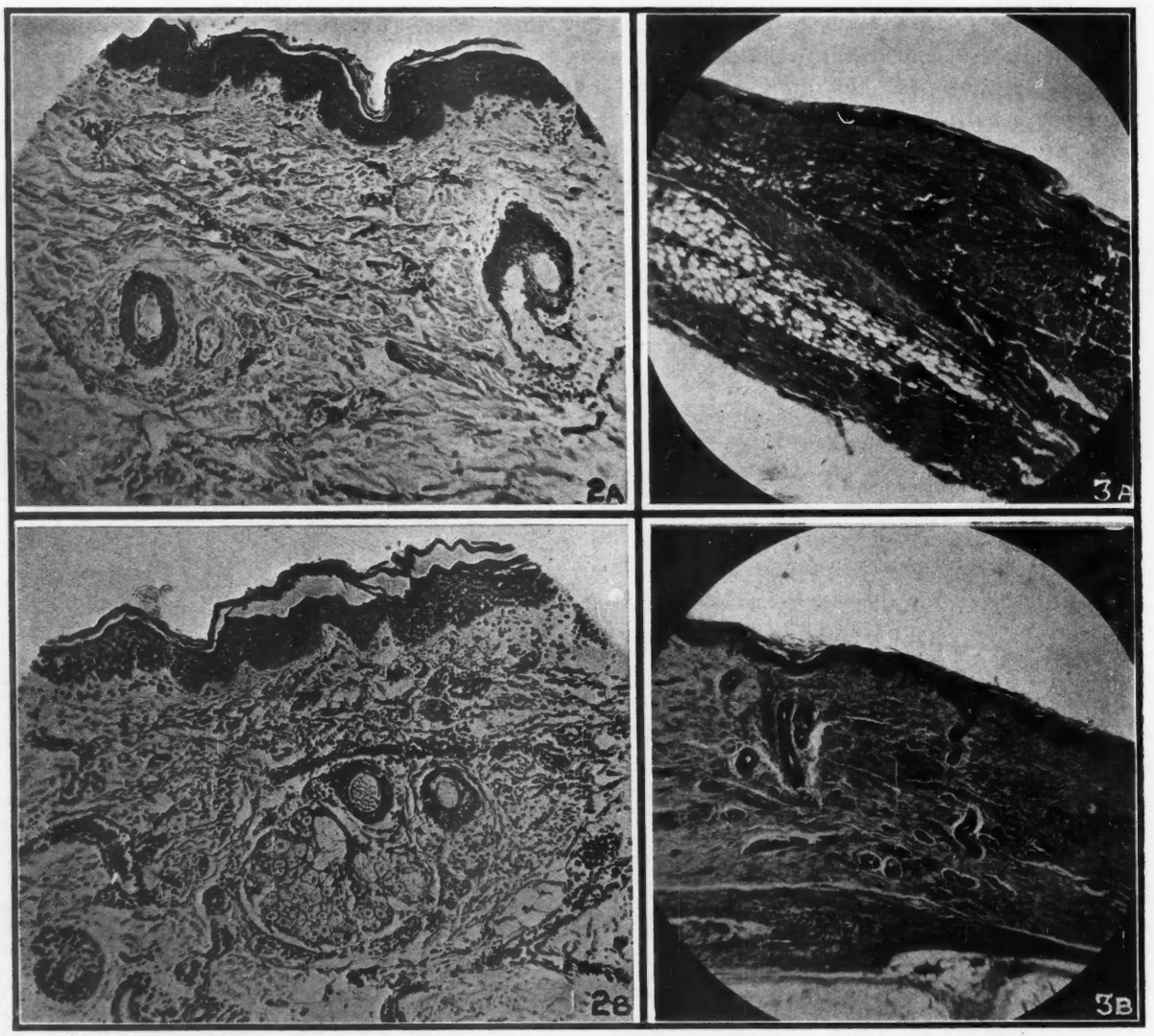

Fig. 2a (Patient 1).—Skin of the pubic region, showing rudimentary sebaceous gland on a hair follicle on one, and a very small one on the other. **Fig. 2b.**—Normal skin control. Baby at full term; sebaceous glands present. **Fig. 3a** (Patient 2).—Breast at nipple in male aged 6 months. **Fig. 3b.**—Normal skin of breast in 2 months' old female infant.

THE BREAST

Patient 1.—The autopsy report states that there was no obvious breast tissue and that the nipples were poorly defined.

Patient 2.—Dr. Wigglesworth took a section through the breast, including the nipple. The block was completely sectioned and no trace of breast tissue was found (Figs. 3a and 3b). Cases have been reported in which the nipples were missing and no breast tissue was palpable, but this seems to be the first time that the absence has been demonstrated microscopically.

Patients 3 and 4.—Nipples were present but breast tissue was not palpable.

THE HAIR

Patient 1.—The hair was sparse, fine, short and fair. There were no eyebrows.

Patient 2.—The hair was white and scanty. The eyebrows were absent and the lashes poorly developed.

Patient 3.—A sparse growth of white hair standing on end. There were no eyebrows and the eyelashes were few in number.

Patient 4.—The hair was light-coloured and rather thin and had abnormal whorls, with irregular direction of the hair slope, *e.g.*, the hair on the left side of the head was directed forward. The eyelashes were pale and fewer in number than normal; the eyebrows were thin, fine and almost invisible until recently. His father, who is a competent observer, was quite positive that a very definite change had occurred in size and in pigmentation of the eyebrows since the use of œstrogenic substances in the nose.

Microscopic sections in these cases seem to confirm the observations made in mice, that in this type the defect is in the hair bulb and is not due to faulty keratinization.

THE NAILS

In all our cases the nails appeared normal.

THE UPPER AIR PASSAGES

Patient 1.—This infant had rhinitis, crusting and mucopus in the nasal cavity, otitis media, and died of pneumonia. An autopsy by Dr. Chase showed a most striking decrease, almost amounting to a complete absence, of the mucous glands of the nasopharynx. A very few small glands were found in the turbinates and a few at the lower end of the trachea, but none in the pharynx, larynx, or the upper trachea. Control sections from normal babies show a great contrast which is obvious to all (see Figs. 4a and 5a; normal controls, Figs. 4b and 5b). In the only two previously recorded autopsies no microscopic examination seems to have been made of the tissues of the nose and throat. Weech,[7] however, in his excellent article forecast some lack of development, and Fleischmann[4] did a biopsy underneath the upper lip which showed no mucous glands.

Patient 2 had a rhinitis, a double otitis media, and died of pneumonia.

Patient 3 had had a constant nasal discharge for years and frequent nose-bleeds. The discharge came away in long string-like masses, frequently followed by bleeding.

Patient 4.—This boy had wide upturned nares. He had some sense of smell. He could detect the smell of a skunk but did not notice that of burning peat. He had had nasal trouble for at least three years. (He is now seven). There were small crusts at first, then larger ones. His nose bled easily. For a year the ozæna had been so offensive that the parents thought that they must shape his life toward some solitary occupation. Treatment by Drs. Mortimer, Wright and Collip according to their method[3] with œstrogenic hormones (Progynon B in oil in this case), immediately produced an amazing and delightful transformation in the condition. This improvement has continued and the father now reports that "the nasal condition has improved almost to a cure, so that now we are using Progynon B very little".

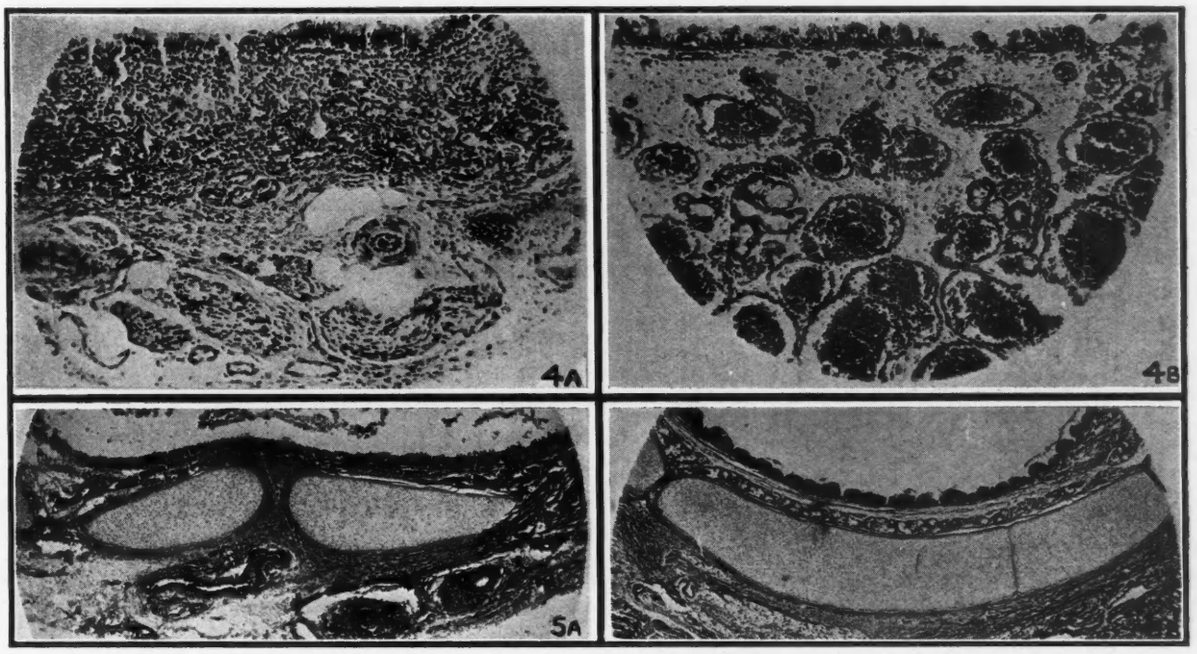

Fig. 4a (Patient 1).—Inferior turbinate. Note the extreme scarcity of mucous glands. **Fig. 4b.**—Normal control of the same age. Note mucous glands between engorged vessels. **Fig. 5a** (Patient 1).—Trachea. Note the complete absence of the collar of mucous glands which lies inside the cartilage. **Fig. 5b.**—Normal control of the same age and at the same level.

Considering that ozæna appears in the earlier years, that it has a familial tendency, that usually there is a dyspituitary state as shown by x-rays of the skull, one is permitted to wonder if, frequently, the basis of ozæna is not hypo-

plasia rather than atrophy. Certainly the cases of dysplasia and ozæna overlap.

Fleischmann,[4] basing his ideas on many measurements of "ozæna skulls", a family tree, and his mouth biopsy findings, comes out flatly in favour of the hypothesis that all ozæna is a part of this hereditary ectodermal dysplasia. This theory is very enticing, but the facts of ozæna are too abominably stubborn for such an all inclusive conception as yet. It does seem rational, however, that many cases of ozæna are a manifestation of an ectodermal defect, if not this particular one.

Endodermal Mucous Tissue

The endodermal mucous tissue was normal in the case which came to autopsy.

Thurnam[5] in 1847 noted a thick ivory-like skull, and this has been confirmed as a feature by nearly all the writers who have considered it since. Patient 4, at seven years, has the characteristic parietal bulges, etc., and, judging by x-ray readings standardized with the penetrometer, the skull is that of a boy five years older. This would seem to indicate dyspituitarism.

Thurnam also found an enlarged thyroid and in our patient 1 Dr. Chase noted an abnormal amount of colloid staining material.

Blood

Thannhauser[6] found a low blood sugar curve in his case. In our patient 3 the sugar tolerance curve was: fasting 76; 30 minutes, 107; 90 minutes, 90; 120 minutes, 68 (see Chart 2); red blood cells 5,030,000; leucocytes 11,800; Hgb. 83 per cent; phosphates 4.23; cholesterol 213; Ca. 11.4.

Internal Secretions

Argument that the glands of internal secretion derived from the ectoderm are involved in both types is as follows. (It is only fair to state that the endocrinologists are by no means prepared to concede that the facts, as set down, constitute proof.)

The anterior lobe of the pituitary body is derived from the ectoderm of the oral cavity, whose tissue we have been able to show by the microscope to be defective.

Adrenal medulla or the adrenotropic factor of the anterior pituitary.—There are low blood pressures and pigmentations in the hydrotic type and this has also been a feature in some cases of the anhydrotic type (Thannhauser).

Diabetogenic factor of the anterior pituitary.—All the blood sugar curves made so far in the hydrotic type run higher than normal and in the anhydrotic type they are lower than normal (see Chart 2).

Gonadotropic factor.—In the hydrotic type there seems to be delayed maturity in the males. The x-ray films show late epiphyseal union in four cases out of four. Voice change began in one boy when he was nearly eighteen. The anhydrotic type in the human cases has occurred so predominately in the male that it is frequently stated that it is sex-linked. Perhaps more truly there is a sex association. In mice the females of the recessive hairless type are usually sterile and the œstrous cycles are less frequent than normal. David says that the sterility or decreased fertility does not seem to be due to defects in the reproductive system of either the males or the females.

Lactogenic factor.—In the hydrotic type the breasts function particularly well. In the other type, while the pituitary connection is admittedly vague, Nature is so serious about this milk business that unless there is a fair amount of sweat gland primordium she suppresses the female altogether and even takes away the breast in the male.

Somatotropic factor.—In the hydrotic type the x-ray shows bone changes suggestive of acromegaly and which can be produced in animals experimentally by the growth factor of the anterior pituitary. There are tufted terminal phalanges, thick skulls, prominent frontal sinuses, and heavy occipital protuberances.

In the anhydrotic type the bones of the skull at least are regularly abnormal.

According to David,[1] homozygous dominant hairless mice, although of normal size at birth, seldom mature, and those which do never attain the normal adult size. Up until the time of birth they have been able to develop normally in regard to size. Following birth, however, they grow only slightly, and the suggestion is made that this may possibly indicate the deficiency of some hormone which had been supplied *in utero*.

The thyrotropic factor.—The hydrotic type usually shows low basal metabolic rates. Anhydrotic cases usually show high rates but the simple lack of sweating may explain this.

Mentality

Patients 1 and 2 were considered somewhat below normal.

Patient 3 was backward physically and mentally.

Patient 4 is quite bright. He learns rapidly and excels his brothers. He keeps his mouth shut curiously, to hide his abnormal teeth, even as the hydrotic patients always try to hide their nails.

SUGGESTED MANAGEMENT

1. Appropriate dental treatment for face, saving physically and mentally.

2. A non-sweating occupation in a moist, temperate climate, with a minimum of present or future worry (*e.g.*, a maritime government job).

3. Œstrogenic substances for the nasal condition.

SUMMARY

Some additional observations are made on the hydrotic types of hereditary ectodermal dysplasia including a chart showing that the average severity of cases has been decreasing.

The first four cases of the anhydrotic type to be reported in Canada are presented with biopsies and the third autopsy on record. The condition is much commoner than usually believed. The distinctive marks are diminished sweating, dental aplasia, and a rhinitis which has usually been called "atrophic". This is shown to be hypoplastic, the mucous glands of the nose and throat being diminished in number or wholly absent.

The resultant lack of defense and air-conditioning, combined with loss of emergency temperature control, is probably a hitherto unrecognized cause of death in infancy. Recognition is not made because death occurs before the children are old enough to complain of the heat and before the distinctive dentition has occurred.

The ozæna responded to the use of œstrogenic substances.

Breast tissue was shown to be absent by the microscope.

The question is raised as to what extent ozæna is a hereditary ectodermal defect.

Evidence is given that the endocrine glands of ectodermal origin are involved in the general ectodermal dysplasia.

I have received every encouragement and cooperation from McGill University and the associated hospitals. Among others at the University to whom I am greatly indebted were Drs. Huskins, Reed, Mortimer and Collip; at the Montreal General, Drs. Rhea, Rabinowitch, Bensley and Wright; at the Royal Victoria Hospital, Drs. Meakins, Cameron Stewart and the late Dr. Chase, who did the autopsy; at the Children's Memorial Hospital, Drs. Cushing, Goldbloom, Burgess, Wiglesworth, for his biopsies, and Childe.

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NEW MENSTRUATION TOILET.—Sir,—During the last few months I have often been asked by young women whether I considered this new practice of plugging the vagina with absorbent tampons instead of using sanitary pads advisable and healthy. My reply is that it is not at all a good thing to do, because vaginal plugs become very offensive and infected even when introduced by the surgeon under the best aseptic technique, and when introduced by a woman herself, under ordinary daily conditions during menstruation, the dammed-up blood in the vagina forms a perfect culture medium, and a profuse growth of septic organisms results. This practice is likely to result in vaginitis, cervicitis, and *B. coli* infections, with quite a possibility of sterility following as well as the other well-known complications of the above conditions. Is it realized how popular this practice is becoming? The "outfits" are procurable at many big stores, and are presented to girls by women who extol their harmlessness and many advantages. For health and beauty classes, dancers, factory girls, etc., they have great attractions, as they require no belt and are comfortable and unseen. The literature accompanying them is all that these young women have to guide them. Quite a lot of doctors seem to be recommending them, but I feel sure that they have forgotten what a vaginal plug is like after its removal; indeed, this is a job usually left to nurses. I shall shortly have a series of reports from bacteriologists on the growths obtained from the discharge before and after the use of these popular vaginal plugs, but in the meantime I think it is only fair to the female public to give some advice on the subject, or is it a matter for the Ministry of Health?—E.L.M. Correspondence in *Brit. M. J.*

EARLY DIAGNOSIS OF CANCER OF THE STOMACH*

BY LOUIS J. NOTKIN, M.D.

Montreal

THE development of x-ray diagnosis in diseases of the stomach has led both clinicians and roentgenologists to hope that with the education of the general practitioner to send his cases to the radiologist cancer of the stomach would be robbed of much of its terror. The burden now lies squarely on the shoulders of the radiologist; what is he doing with his opportunities? Statistics indicate that even in excellent x-ray laboratories correct diagnosis is not made in anywhere near the 100 per cent mark; elsewhere the figures are necessarily much lower. While admitting the inevitability of the occasional blunder, it is maintained that greater diligence on the part of the radiologist, more adequate cooperation with the physician, and a careful re-study of wrongly diagnosed cases would help considerably in lowering the percentage of diagnostic error in this type of case.

The criterion of cancer of the stomach is a filling defect, and when this is so pronounced that a mere tyro in the field of radiology has no difficulty in making the correct diagnosis the case is frequently beyond surgical relief. To await such advanced manifestations is comparable to waiting for the classical signs of cachexia, a palpable mass, and evidence of metastases before making a clinical diagnosis. The recognition of small, early lesions is not attainable without extreme care and diligence, even by radiologists of great experience. Such lesions are filling defects, but they are easily confused with localized spasm, perigastritic adhesions, pressure defects from without, abnormally coarse rugæ, etc., because they are slight in extent and depth. The radiologist must satisfy himself completely that such irregularities are produced by non-malignant lesions before so committing himself. This frequently means not only a very careful study of such cases but also repeated examinations and the exhibition of considerable technical ingenuity.

In a comparatively short period of time the author has seen an unusually large number of cases which were wrongly diagnosed as "negative" by the radiologist. In three of these, slight but unmistakable evidence of organic changes was present. The correct diagnosis was finally made when surgical procedure was a forlorn hope. In all the lesions were situated in resectable portions of the stomach. These cases are being reported as examples illustrative of the type of case under discussion; the fourth is a case of linitis plastica which the author followed for a period of three years before realizing that he was dealing with a slowly developing malignant lesion.

CASE 1

Mr. A., aged 43, November, 1934. At this date he was seen by his physician for the following complaints: pain in the epigastrium, of one year's duration, burning in character, occurring usually at varying times after meals and occasionally at night, very severe, and radiating to the back at the level of the lower ribs; vomiting, which relieved the pain; a loss of 12 lbs. in the preceding three months.

Past history.—Typhus 26 years ago; herniotomy for epigastric hernia in 1911; lead poisoning in 1929 (painter).

Family history.—Irrelevant.

Physical examination.—Some evidence of loss of weight; temperature 98.2°; pulse 58; blood pressure 104/80; tenderness at the site of the herniotomy scar.

Three possible diagnoses were made by the physician—lead poisoning, gastric ulcer, carcinoma of the stomach. Radiological examination of the stomach revealed persistent spasm of the greater curvature in the prepyloric region, a 10 per cent six-hour delay, and a slight degree of irregularity of the lesser curvature not directly opposite the site of the spasm. Re-examination within three weeks was requested by the radiologist, since he could not commit himself to a definite diagnosis at the time. The patient was placed on a Sippy regimen, and, apparently improved, did not return to his physician until seven months later. A barium series repeated at this time by another radiologist was reported as entirely negative, although the evidence in favour of an organic lesion was now more pronounced than in the first examination. With this reassurance the physician in charge of the case apparently considered the symptoms to be functional and prescribed a bromide mixture. The patient made his next appearance ten months later, complaining, in addition to the previous symptoms, of left abdominal pain suggesting renal colic. There was an additional loss of 20 lbs. in weight. The lower abdomen was soft; the upper abdomen was moderately resistant; and a mass was readily palpable in the left upper quadrant. Laboratory findings: urine, specific gravity 1.010; albumin a faint trace; no sugar; red blood cells 3,960,000; white blood cells 16,050; Hgb. 61 per cent. Test meal: fasting contents 60 c.c.; free HCl 0, 0, 6, 6, 8; total 8, 8, 20, 10, 16, in specimens taken at 15-minute intervals. A strongly positive occult blood reaction was given by all specimens. Radiological examination revealed an extensive lesion of the distal half of the stomach. Operation was considered inadvisable. A month later the patient developed severe colicky pains associated with vomiting and tarry stools.

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The pulse was thready at 120; blood pressure 68/48; temperature 98.4°; red blood cells 3,285,000; white blood cells 21,650; Hgb. 60 per cent. Within a day the temperature rose to 103.4°, the abdomen became rigid and tender, and the patient expired within two days after the onset of the above symptoms. A diagnosis of probable perforation of the stomach through a cancerous lesion was made. There was no autopsy.

Figs. 1, 2 and 3 indicate the successive stages in the development of the disease. What appeared to be a persistent spasm on the greater curvature, as reported by the first radiologist, persists in the second series of films taken seven months later. Reference to Figs. 11, 12 and 13, however, indicates the probability that the apparent spasm was really an organic change produced by shortening of the involved circular muscle fibres, extension of the process leading ultimately to marked narrowing of the distal end of the stomach. Comparison of the figures shows clearly the evolution of the "spastic" area into the centre of growth on the greater curvature. It is also interesting to note that the vertical band of decreased density caudad to the apparently spastic area persists, retains its position, and becomes larger in the successive examinations.

CASE 2

Mr. B. The patient had been subject to recurrent attacks of indigestion for many years. In March, 1935, when he was 66 years of age, the symptoms became more persistent and more troublesome, and on July 4th he subjected himself to a radiological examination of his gastro-intestinal tract. The findings were reported "negative". Reassured by this, the patient accepted the symptoms as being due to an exacerbation of his old "indigestion". He was comparatively well on a restricted diet and frequent small feedings until May, 1936, when he began to complain of epigastric distress after meals, lasting ½ to 1 hour, nausea and, on several occasions, vomiting. Within a month he returned to the same radiologist who found extensive malignant involvement of the stomach. On examination at this time the following positive findings were elicited. Blood pressure 100/80; pulse 72; temperature 98.4°. The abdomen was full and soft, except in the epigastrium, where some resistance was encountered as well as a suggestion of a mass. The histamine test meal showed an absence of free HCl in all except the 1-hour specimen, in which it was 10; the total acid values ranged from 7 to 19 in the four 15-minute specimens. The benzidine reaction was strongly positive in all. Red blood cells 5,220,000; Hgb. 83 per cent. Occult blood was present in all stool specimens.

Laparotomy revealed the presence of a large mass infiltrating the whole circumference of the stomach and leaving only a small portion of the fundus intact. The peritoneal surface of the anterior wall of the stomach was studded with metastases; the gastro-colic omentum was filled with large red vascular masses. A small subperitoneal nodule was found on the right lobe of the liver. The stomach was fixed and immobile. The abdomen was closed.

Reference to Figs. 7, 8, 14 and 15 will clearly show that enough radiological evidence was present fully a year prior to the operation to at least warrant further studies at that time.

CASE 3

Mr. C., aged 66, May, 1936. The patient was well up to 15 months before being seen, when he began to be troubled with occasional nausea and some time later with excessive salivation. During the preceding 10 months there had been gradually increasing anorexia; bitter taste in the mouth; a sense of fullness in the epigastrium; vomiting of bile-stained fluid; weakness, and a rapid loss of weight during the preceding three weeks. His average weight in health had been 132 and had gone down to 106. He had been subjected to x-ray examination with barium twice within the previous year. The first examination was reported "negative"; the second led to a suspicion of possible malignancy, and two months later the patient was sent elsewhere for investigation, with the following results. He showed definite evidence of marked loss of weight, but was not anæmic or cachectic. A few moist crepitations were present at both bases. The heart was slightly enlarged to the left; blood pressure 130/90; pulse 90. The abdomen was soft and flat; the abdominal wall was thin. Epigastric and right inguinal herniæ were present. There was no palpable mass in the epigastrium. Urine: specific gravity 1.014; albumin, a trace; glucose 0; red blood cells 4,480,000; white blood cells 7,200; Hgb. 70 per cent. The stool was examined for occult blood on one occasion only and was then negative. Gastric test meal: (15-minute intervals for 1 hour) free HCl (fasting 0), 0, 10, 18, 6; total acidity (fasting 8), 12, 24, 30, 18. Traces of occult blood were present in all specimens. Clinical impression: carcinoma of the cardiac end of the stomach, with possibly early involvement of the terminal œsophagus. Radiological examination, Figs. 9, 10, 16 and 17, revealed the presence of an extensive deformity of the stomach beginning at the cardia and involving two-thirds of the stomach.

CASE 4

Mrs. D., aged 52, January, 1927. During the preceding 10 years the patient had suffered from periodically recurring sensations of pressure in the epigastrium and behind the sternum, associated with pain between the shoulder blades. A change in the symptoms occurred in the preceding two months. The above symptoms were replaced with a burning sensation in the epigastrium occurring shortly after eating and relieved by a glass of hot water; belching; vomiting on several occasions immediately after meals; and a loss of appetite. There had been some little loss of weight during the preceding 10 years, but the weight had remained constant for some months. No loss of strength; no undue fatigability. The bowels were sluggish. She had not had any serious illnesses in her life. Occasional amenorrhœa of one month during the preceding year and a half. Otherwise the personal and the family histories were irrelevant.

At this time the patient was well-preserved, appearing to be considerably younger than her age and in excellent health. Physical examination revealed no noteworthy departures from the normal. Weight 165 lbs.; pulse 72; blood pressure 125/80. Urine: specific gravity 1.015, no albumin and no sugar. A moderate reaction for occult blood was present in the stool.

Barium series: a somewhat long stomach with an irregularity and an indentation of the greater curvature involving its upper half. This was considered to be due to contraction of the muscularis mucosæ and to pressure by the splenic flexure. The cap was definitely larger than normal. At the six-hour examination the advance of the meal was within normal limits. The barium enema revealed no abnormalities of the colon.

The stool was examined on several occasions and always gave a weakly to moderately positive benzidine reaction. Proctoscopic and sigmoidoscopic examination revealed the presence of external and internal hæmorrhoids which did not show any evidence of recent bleeding. The patient refused the test meal.

The diagnosis at this time was: chronic cholecystitis; probable hypochlorhydria; colonic stasis; in-

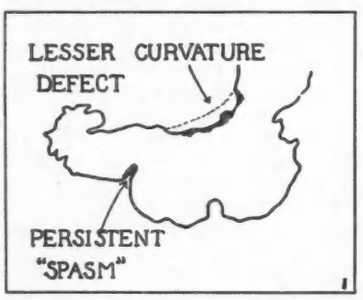
ternal and external hæmorrhoids. The presence of occult blood in the stools could not be definitely accounted for. The patient returned a month later stating that she was better, but complaining of a new symptom, nausea. She had lost an additional 5 lbs. in weight. On this occasion the liver was found to be just palpable.

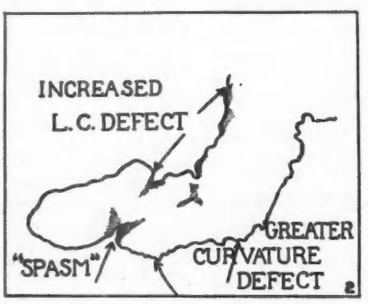
October, 1928.—A sense of fullness in the epigastrium after the smallest meals and a return of the old symptoms. Occult blood was found in two stools examined.

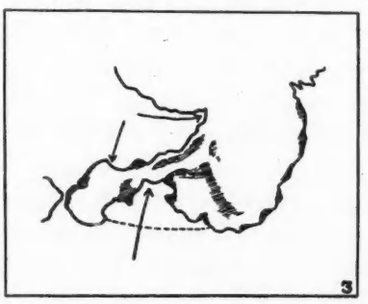
April, 1929.—Crampy pains in the epigastrium two hours after meals, penetrating to the back and radiating to the left upper quadrant, associated with chills. The temperature was normal. An additional loss of 4½ lbs. in weight. Cholecystography: a large, faintly filling gall bladder, concentrating moderately well, and emptying completely after a fat meal. Barium series: no essential change from the previous findings.

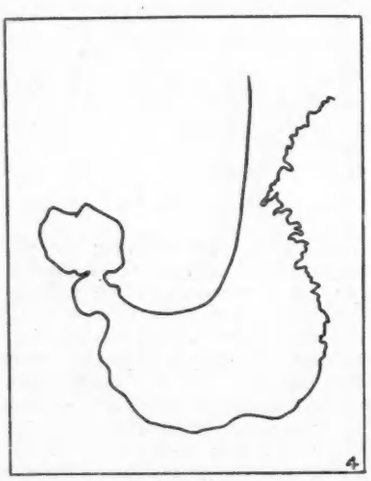
July, 1929.—The patient reported that she had been better. An additional loss of 5 lbs. in weight. The heart was slightly enlarged to the left, with a soft systolic murmur at the apex. Blood pressure 155/75; pulse 66.

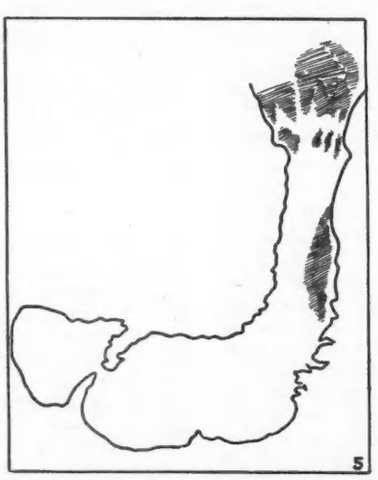
April, 1930.—She had a fainting spell preceded by nausea. Temperature 98.4°; blood pressure 110/70. Moderate pallor. Red blood cells 3,940,000; Hgb. 60

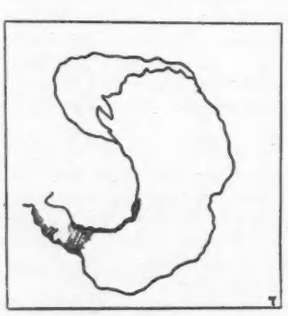


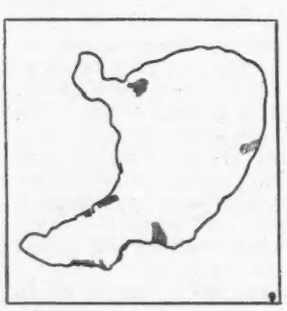


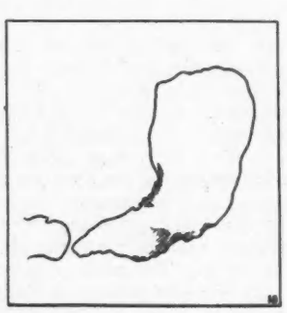










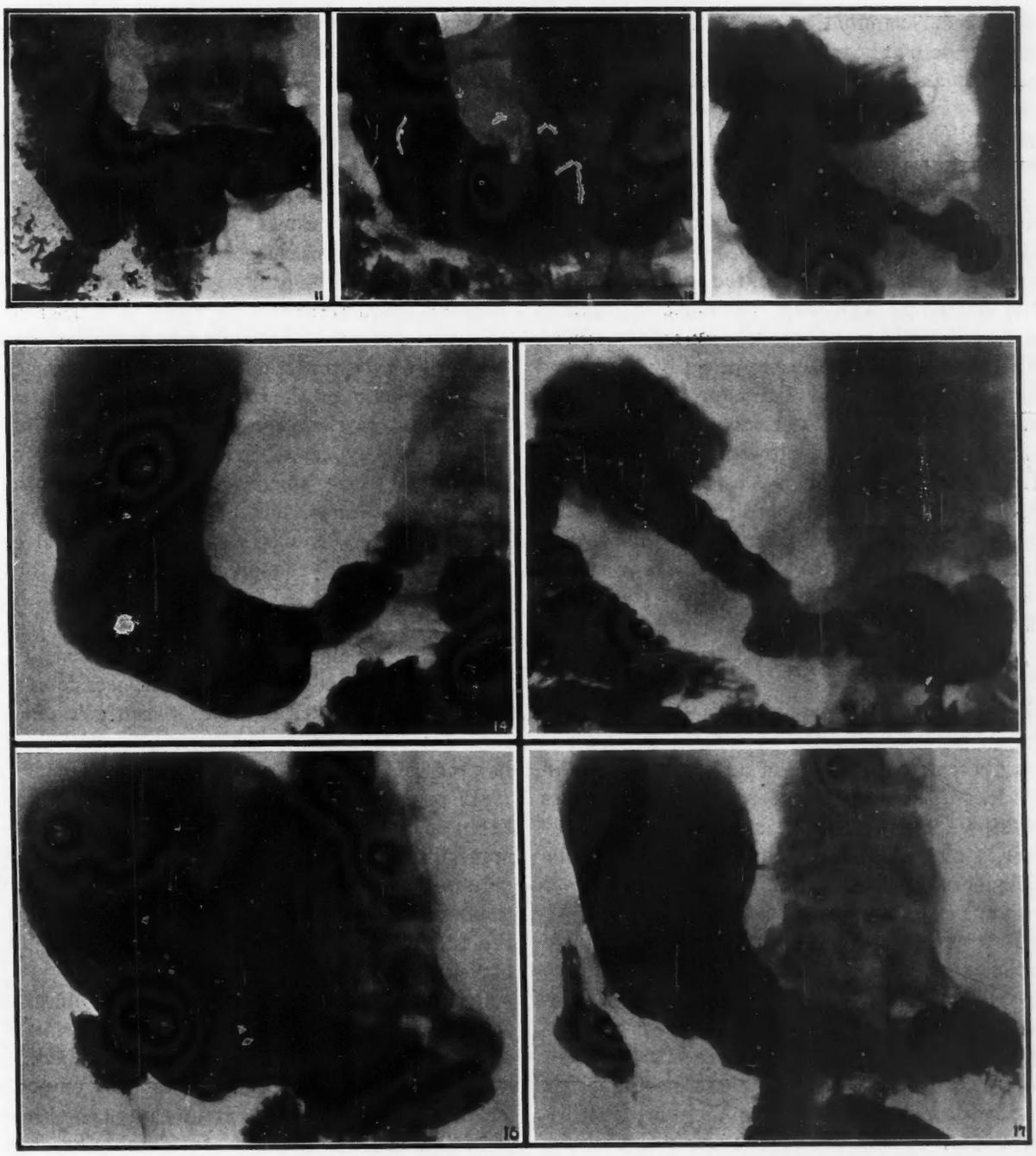


per cent (Sahli). The following day a dark stool was passed which gave a four-plus reaction for blood. Within a week the stool was free from occult blood and two weeks later the patient was again subjected to a barium series. The stomach was definitely smaller than in the previous examinations. Both curvatures were definitely irregular and the stomach was markedly narrowed in its entire length. At the six-hour examination about 30 per cent of the meal was retained in the stomach. A diagnosis of malignant infiltration of the stomach, possibly linitis plastica, was made.

January, 1931.—Nausea, vomiting, pain in the epigastrium. Unless she ate very slowly there was a sense of fullness in the epigastrium and some difficulty in swallowing. Increasing weakness. Occasional hiccough. A gnawing sensation in the epigastrium, relieved by food. Weight 130 lbs. A mass, the size of an orange, was palpable in the epigastrium. In July ascites and marked œdema of the legs, extending to the hips, developed, with death intervening in September, 1931.

The interest of this case, apart from that indicated by the purpose of this paper, is the long history (the patient dying four years and nine months after seeking treatment), as well as the periodic x-ray examinations beginning almost from the onset of the symptoms and continued

to the time of marked involvement of the stomach. There is no doubt, in retrospect, that the patient was suffering from carcinoma of the stomach at the time of the first examination, as evidenced by the persistent presence of occult blood in the stools, the progressive loss of weight, and the continuous aggravation of symptoms. In the first roentgen examination of the stomach the only evidence of abnormality was present in the greater curvature which was originally interpreted as being mainly due to pressure from without. In the light of the subsequent examination which revealed more definite changes in this region suggestive of organic disease the author believes it may be taken for granted that the lesion originated in this area and was present at the time of the first examination. It is possible that studies of the mucosal relief at that time might have then revealed the true nature of the disease (see Figs. 4, 5 and 6). The radiologist must learn to recognize such early signs if anything is to be accomplished toward increasing the number of "cures" in cancer of the stomach.



(NOTE: the skiagrams are reversed)

X-RAY STUDY

X-ray investigation of the gastro-intestinal tract is probably the most difficult division of radiological diagnosis, and even the most expert radiologist occasionally falls into error. Certain points, to be discussed below, help considerably in avoiding pitfalls.

Preparation of the patient.—If the two-meal method of examination is employed the examination must be repeated after a fast of approximately 12 hours if the barium taken prior to the examination interferes in the least with perfect visualization of every part of the stomach. The single meal examination is preferable, and should always be employed when one is searching for early manifestations of organic disease. If secretion is present in the stomach to a definitely perceptible extent the stomach should be evacuated before the examination.

Mucosal visualization.—The mucosal pattern and detail should be carefully examined in each case. Such details can be brought out only by exerting graded pressure on the stomach through the abdominal wall when the stomach contains a very small quantity of the contrast medium. This pressure can be accomplished by the gloved hand, the Holzknecht distinctor, or one of the various compressing devices used in mucosal radiography. Proficiency in the use of the Holtzknecht distinctor goes a long way in making up for the lack of expensive apparatus. The mucosal detail made perceptible in this fashion frequently demonstrates deviations from the normal which are so slight as to be completely obscured by a full barium meal.

The silhouette of the gastric lumen.—The filled stomach may give confirmation of the mucosal relief findings as well as additional information. The gastric silhouette as a whole may reveal the presence of an organic lesion in the loss of the normal graceful flow of the curves presented by the healthy stomach. This, however, is a comparatively late manifestation. The silhouette should be examined from all angles by appropriate rotation of the patient.

Irregularities of the greater curvature are frequently passed by as unimportant, yet these may represent early malignancy (Case 4). The greater curvature is frequently the site of irregularities produced by contractions of the muscularis mucosæ. Since these irregularities are not constant in contour they are readily recognized by comparing the involved area in a series of films taken during one, and, if necessary, more than one examination. If the irregularities are persistent and retain the same outline, either in part or in whole, they must be considered organic until this view is definitely established or disproved. Films for comparison must all be taken in the same position and with the same angulation of the tube. Such lesions, if early, need not necessarily lead to localized absence or undue shallowness of peristaltic waves. Irregularities in the contour of the greater curvature produced by pressure from without are more readily recognized and should present no difficulties.

The lesser curvature should be very carefully examined as it is frequently the site of malignant lesions. An irregularity in its sweep may be noted, such as a small section exhibiting a double contour (this must be differentiated from thickened rugæ which sometimes present a similar appearance on the greater or lesser curvatures), persistent flattening of a short stretch of the curvature, giving the impression of undue rigidity, or a small niche. An important characteristic of a niche produced by ulceration of a malignant lesion is that it does not project beyond the lumen of the stomach unless it occurs on the base of a previous gastric ulcer, and, further, compression of the region will frequently reveal evidence of swelling or heaped-up tissue about the periphery of the niche on the lumen side. This manifests itself, under pressure, as a crescentic area unfilled or partly filled with barium suspension, which thus outlines the lumen side of the ulcer against the rest of the stomach.

Annular carcinoma of the stomach usually presents no great difficulties, but occasionally prepyloric irregularities are quite confusing and difficult to interpret. Such irregularities may be produced by spasm associated with prepyloric ulcer or with gall-bladder disease, or in films taken in the prone position, by pressure of the spine. The last is readily excluded; the former may prove quite difficult of accurate interpretation and may require repeated examinations and the full cooperation of the patient's physician to clear up.

Occasionally, one-finger compression of the antrum will indicate the presence of infiltration of the anterior gastric wall, or of a mass jutting into the lumen from either the anterior or posterior wall. Under such circumstances the area of barium expressed will be considerably greater than seen under normal circumstances. If very

pronounced this sign frequently indicates advanced disease.

DISCUSSION

These cases illustrate definitely certain points. In case 1 the diagnosis was made 10 months after the first examination; in case 2, 15 months; in case 3, 3 months; in case 4, 27 months. In all the diagnosis could and should have been made earlier.

Review of the radiograms in all cases indicated the presence of suggestive abnormalities which were ignored at the time of the first examinations, except in case 1, in which at a subsequent examination another radiologist passed upon them as negative.

In these cases the evolution of the radiological signs, as followed in successive examinations, clearly indicates the significance of these irregularities.

If the radiologist is to be of help to the clinician in the "war" on cancer he must recognize early lesions as seen in the first examinations of these cases or in repeat examinations done within reasonable periods.

The radiologist must be constantly aware of the great responsibility in dictating his final report. It is much better to confess that he "does not know" than to give a "negative" report. This lulls both patient and physician into a false sense of security, and the patient loses the opportunity for a correct and still early diagnosis at a later, not-too-distant re-examination. The clinician is also remiss in too frequently accepting the "negative" report of the radiologist; the clinical picture should surely have a bearing on the final diagnosis.

SUMMARY

Four cases of carcinoma of the stomach in which the x-ray diagnosis was made too late to be of service are reviewed. The progressive changes in the roentgenograms, from early, easily misinterpreted lesions to the full-blown easily-recognizable stages, are demonstrated.

A plea is made for recognition of the early signs as demonstrated in the first roentgenograms of these cases.

Diagnostic roentgen methods and criteria are briefly discussed.

CYSTIC DISEASE OF THE URINARY TRACT EPITHELIUM*

(WITH REPORT OF A CASE)

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London, Ont.

ALTHOUGH cystic disease of the urinary tract has long been observed, relatively few cases have been diagnosed clinically, and the etiology remains not entirely clear. The original gross description was by Morgagni[1] in 1761, and the first microscopic study was by Litten[2] in 1876. Since these reports many papers have been written on the subject, discussing the etiology, and reporting more than 70 cases. The theories suggested include (1) retention of secretions in glands, or (2) in the mucosal crypts, (3) the encystment of parasites, and (4) post-inflammatory changes.

The first of these theories was abandoned when it was established that the upper urinary tract is devoid of gland structures. The second possibility, that of sealing over of folds or crypts in the mucosa, has remained worthy of consideration until recently (see Morse[3]). The parasitic origin of the cysts was suggested by Eve[4] and Sutton,[5] who found small ovoid bodies in some of the cysts. These "psorospermial bodies" later proved to be inspissated material secreted by the cyst wall, bearing only a superficial resemblance to protozoan parasites (see Fig. 1).

The inflammatory nature of the cysts was suggested by von Brunn[6] in 1893, and has been supported by the majority of investigators since that time. This mechanism involves budding of the epithelium downward into the submucosa, by overgrowth of the basal layers in response to inflammation. These epithelial buds are then amputated by proliferating fibrous tissue, leaving an isolated nest of cells; and, finally, the centre of the cell-nest softens and liquefies, forming the cyst. Enlargement may continue by the shedding of epithelial debris into the lumen, the size being limited by the surrounding tissue, and as it enlarges the

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cyst may project itself beyond the surface of the bladder mucosa. Various workers have confirmed the frequent presence of such epithelial buds and nests along the urinary tract, although not all agree that these forms arise in response to inflammation, some holding that they may occur as congenital "rests".

The most complete modern study in this regard is that of Morse.[3] This author found epithelial buds, nests, or microscopic cysts, in 108 (or 86 per cent) of 125 consecutive autopsies studied by serial section of selected areas; only 3 cases had macroscopically recognizable cysts. Evidence of inflammation was found in 65 (or 58 per cent) of the 108 cases mentioned, and in 4 (or 24 per cent) of 17 cases in which no such changes were found. No glands were found above the level of the trigone of the bladder. The apparent anomaly of the frequent microscopic finding of cysts was, of course, due to their very small size and to masking by accompanying inflammation.

That cystic disease occurs with a variety of inflammations there can be no doubt. Cystitis cystica has been described in association with chronic cystitis due to a wide variety of bacteria,[3] and accompanying bilharziasis of the bladder,[7] and tuberculosis of the bladder.[8] Renal calculi are frequently found with pyelitis cystica. Epithelial nests and microscopic cysts are common in the chronic urethritis of the female. On the other hand, cysts are sometimes, albeit rarely, found in children, and Marckwald[9] has described a typical case in a new-born infant. This author reasoned that inflammation was not the cause in this case, although Herxheimer,[10] some ten years later, explained away this contention by assuming the excretion of some toxic material in the urine. A further objection to the assumption that von Brunn's cell-nests are inflammatory is constituted by the numerous cases of widespread cystic disease in which no history of a previous urinary tract inflammation can be obtained. In Morse's series for example, a large number of the cases with buds, nests, or cysts showed no evidence of an inflammatory reaction when examined.

The only experiments on the problem are those of Giani[11] in 1906. This worker found typical epithelial buds, nests, and cysts in rabbit bladders after contact for some weeks with a foreign body, or after curettage. The cysts later disappeared spontaneously by rupture into the bladder, healing without a trace.

Cystitis cystica is not commonly observed by cystoscopy, and pyelitis cystica and ureteritis cystica were reported as clinically diagnosed only 4 times when Hinman *et al.*[8] in 1936, reviewed the literature and added 3 new cases. On several occasions cysts have been diagnosed as non-opaque stones, and nephrectomy done. Hinman's cases of ureteritis cystica were treated, as suggested by Kindall,[12] by rupture of the cysts by passing a large ureteral catheter, and then applying silver nitrate solution.

In the present report, a case of cystic disease of both pelves, both ureters, and the bladder will be described.

CASE REPORT

Mr. J.T., a white male of 48 years, a farmer, was first seen on March 18, 1937, complaining of "red urine" at intervals for one month. No stones had been passed, and no large clots of blood; there had been no colic, no difficulty with urination, and no previous history of any bladder symptoms. Several years before he had had "gas on the stomach", with vague abdominal pains, which had never been noted in either loin, and this had recurred 2 or 3 weeks before admission.

There were no relevant findings on physical examination, and the prostate gland was normal. The urine was red, containing 100 red blood cells and 3 to 5 white blood cells per high power field.

Cystoscopy revealed very slight benign prostatic hypertrophy, with no residual urine. On the trigone, near the bladder neck, were numerous cysts, varying in size from a pin-point to about 4 mm. in diameter. Some were translucent, others were filled with an opaque yellowish material. The dome was free from cysts, and showed only a slight thickening. Blood was seen issuing from the right ureter. This ureter was easily catheterized 30 cm., but the left ureter could be ascended only 10 cm.

Retrograde pyelograms, the left one being made at a second cystoscopy, showed beading of both ureters, and the deformity of the pelves described as characteristic of pyelitis cystica by Hinman[8] (see Fig. 2). There was no evidence of stone in the plain films. Cultures showed *S. viridans* in the urine from each ureter and from the bladder. Guinea-pig inoculations were negative for tubercle bacilli.

Transurethral resection of the cyst-bearing area in the bladder was done, and No. 10 catheters were passed up each ureter, and 1 per cent silver nitrate instilled. Subsequent cystoscopy (May 11, 1937) showed incomplete healing, and no recurrence of the cysts. There was occasional bleeding until June, 1937, but since that date only one episode has occurred, and the patient is now symptom-free.

The fragments removed at operation were sectioned and showed numerous cysts of various sizes and of various degrees of maturity (see Fig. 4). Occasional von Brunn's nests were seen (as in Fig. 4). The cysts had transitional epithelial walls, usually several cells thick. These cells were compressed and flattened in most of the larger cysts, but appeared secretory in several smaller cysts, being elongated with peripheral nuclei. The cysts contained an amorphous fluid, with scattered or dense accumulations of polymorphonuclear and/or round cells. About the cysts was a dense infiltration with round cells and a few eosinophiles, and in the submucosa near the cysts were a number of lymphoid follicles with germinal centres (cystitis lymphomatosa). Dilated lymphatics stood out unusually well in the deeper layers.

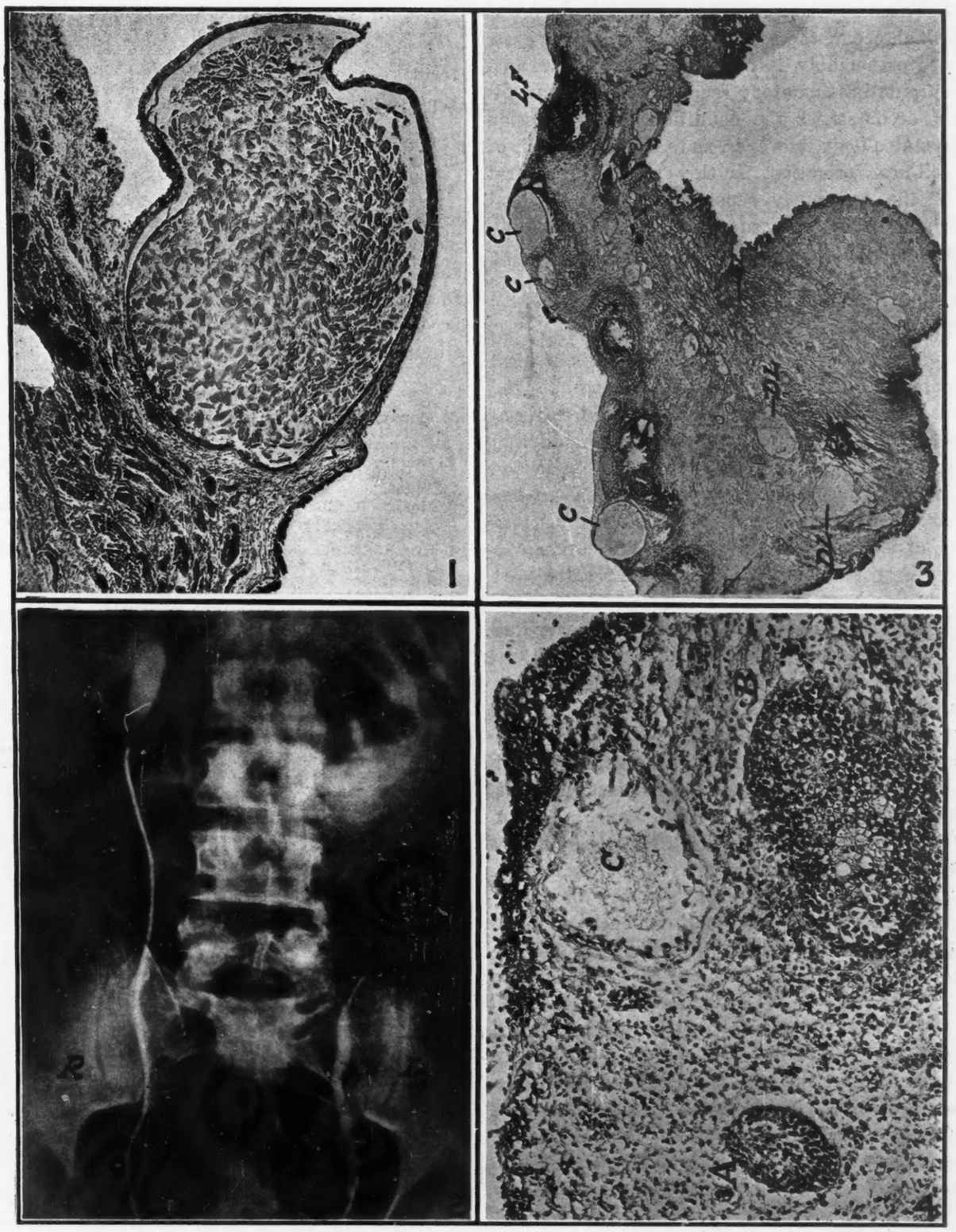

Fig. 1.—Cyst from autopsy case No. 3674, showing inspissated debris in the cyst lumen of the type which was thought to be parasitic "psorospermial bodies" by Eve and Bland Sutton. **Fig. 2.**—X-ray characteristic of pyelitis cystica, showing (R) the dilated renal pelvis with constricted infundibula and narrowed ureteropelvic junction, and (L) multiple filling defects of the lower ureter (arrow). The left pyelogram showed similar changes. **Fig. 3.**—Photomicrograph of fragment removed at biopsy of clinical case. Note the cysts of various sizes (C), the marked lymphoid infiltration (LF), and the dilated lymphatics in the deeper layers (DL). **Fig. 4.**—Photomicrograph from clinical case, showing (A) a typical cell-nest of von Brunn, a cell-nest (B) in which central liquefaction is occurring, and (C) a small cyst.

This case illustrates the variety of cyst-forms which occur, the cell-nest from which the cysts are presumably formed, and the well marked chronic inflammatory reaction which frequently accompanies the condition. The question remains open, however, as to the mechanism of cell-nest formation. In this case and in several of the previously reported cases no clinical history of an antecedent inflammation was obtainable. And the case of Marckwald in the new-born infant seems unsatisfactorily explained on the basis of a possible toxic material in the urine.

That the urinary tract epithelium is at least potentially secretory is well known to the urologist, as evidenced by the mucoid material which may be poured out from the bladder in response to an indwelling catheter or in the cases of so-called "catarrhal" cystitis. It has also been shown that when the bladder mucosa is experimentally transplanted in animals a cystic space filled with a thin fluid results.[13] It has also been shown that the secretion is increased when there is increased vascularity due to inflammation (Stoerk and Zuckerkandl[14]).

Because of the objections to the inflammatory origin of the cell-nest mentioned previously it would seem quite likely that, as has been suggested, the cell nests may occur as congenital "rests". Low-grade chronic inflammation might still be considered the usual cause of cyst formation from the nests, by initiating or enhancing the secretory activity of their cells, but other growth stimulants could have the same effect, and in this way the occurrence of cystic disease in the new-born, or without inflammation, is explainable.

SUMMARY AND CONCLUSIONS

1. A case of cystic disease of the urinary tract, diagnosed clinically, and biopsied, is reported.

2. The theories of the etiology of the disease are reviewed, and the cell-nest hypothesis of von Brunn discussed.

3. It is suggested that cell-nests may occur as congenital "rests", rather than only as a response to inflammation, and that cysts may form from such rests when epithelial secretion is excited by inflammation or other growth stimuli.

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GENERALIZED VACCINIA.—J. D. Rolleston who records an illustrative case, states that vaccinia is a rare condition, and with a few exceptions is found exclusively in children. The following statistics indicate its rarity in different countries. France, six to eight cases among 500,000 to 600,000 vaccinations; Germany, fifty to sixty cases in 2,285,578 vaccinations; and Denmark, four cases among 39,915 vaccinations. As a general rule the prognosis is good, and the condition is only likely to be serious, and even fatal, when it supervenes on a pre-existing dermatosis, especially eczema, seborrhœic dermatitis, or impetigo. According to modern views generalized vaccinia is due to a hæmatogenous outcropping of the virus of the vaccine which enters the blood stream even when vaccination follows its usual course. Its rarity is due to the fact that the balance between the virus and the virucidal substances in the blood is not often disturbed in persons with an intact skin, whereas eczema and other pre-existing dermatoses are liable to upset this balance. Rolleston's case was that of a male infant, aged 7 months, who developed a generalized vaccinial eruption after a single insertion of Government lymph. The lesions, though generalized, were sparse, the face and trunk being little affected. There was no constitutional disturbance, and apart from a severe attack of gastro-enteritis recovery was uneventful.—*Brit. J. Child. Dis.*, July-September, 1937, p. 187. Abst. in *Brit. M. J.*

INTRA-NASAL ADMINISTRATION OF ŒSTROGENIC HORMONES IN CONSTITUTIONAL DEAFNESS*

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IN an earlier publication,[1] in which we drew attention to the beneficial effect of the intra-nasal administration of œstrogenic substances in atrophic rhinitis and ozæna, mention was made of the fact that a female patient suffering from constitutional deafness as well as atrophic rhinitis had reported improvement in tinnitus and in hearing during treatment. Attention was also drawn to the fact that there had been found in that series of cases 6 females and 1 male who suffered from two constitutional disabilities, namely atrophic rhinitis and progressive deafness.

This had led at that time to the examination of the cranial skiagrams in 70 cases of constitutional deafness, from which it had become clear that there was to be found in patients suffering from the ear-defect a constitutional background in certain respects similar to that reported as occurring in the nasal condition. The inference was drawn from these facts that there might be a relationship between the two conditions themselves or in the constitutional background in which these defects were apt to appear, and it was hoped that further knowledge of the nature of such relationships might be of value either in clarifying the etiological concept or in actual treatment of the more obscure condition. It was suspected at that time that there might exist a hitherto unrecognized "oto-genital" relationship which, although possibly dating far back in phylogeny, might still play a part in the physiology of hearing in man. Although such a relationship is under investigation we have at the moment no direct evidence to offer in this regard. Cases of constitutional deafness have been treated in the Department of Oto-Laryngology of the Montreal General Hospital by intra-nasal application of œstrogenic substances since July, 1936, and the object of this paper is to report the results of this empirical treatment in our hands, in view of the interest which this work has aroused amongst those otologists who have had knowledge of it.

The series investigated consists of 153 patients of whom 94 are females and 59 males. The average age of the females is 37 years, the youngest being 11 years of age and the oldest 74; in the males of the series the average age is 39 years, the youngest male being 9 and the oldest 76.

While present physiological characteristics are highly important in estimating the constitutional nature of a given individual or that common to a group of individuals it has been shown[2] that the cranial skiagram is a datum of authority in estimating the relative influence of those metabolic factors which largely determine morphological or constitutional type. Recognition of the significance of the cranial data in a group of cases of atrophic rhinitis led us to the recognition of the specific relationship between the sex glands and the nasal mucosa, both in man and other primates.[3, 4] This in turn led to a new treatment of atrophic rhinitis and ozæna of undisputed value, a fact fully confirmed recently elsewhere.[5]

The facts that the two diseases may occur in the same individual and that treatment directed towards the specific relief of the nasal condition may benefit the aural condition make the comparison of the cranial data in the two groups a matter of considerable interest, since the possibility arises that a factor in the etiology of both diseases may be a common constitutional disability. Since cranial type is a reliable index of constitutional type it follows that one might expect to find a closely similar type distribution in the cranial skiagrams in the two diseases. This supposition has proved to be well founded.

Considering first the *females* in the two groups (Table I) it is no disadvantage that the total number in constitutional deafness is twice that in atrophic rhinitis. It is obvious that the two groups closely resemble each other. Both show the same large proportion of cranial dysplasia.

The majority of women in both groups show the hypofunctional aspect of dyspituitarism in the ascendant. In atrophic rhinitis three-quarters of them show earlier or later hypopituitarism (Types III, IV and V) and in

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constitutional deafness this is only slightly less well marked. There are, however, two significant differences. First, under-development of the facial part of the skull (Types III and IV) is about twice as frequent in women with atrophic rhinitis as in those with constitutional deafness, and, second, sclerosis of the calvaria supervening after adequate growth of the brain-case and face, a premature senile change occurring after dimensional growth is over (Type V), is twice as common in constitutional deafness as in atrophic rhinitis.

TABLE I.

CRANIAL DYSPLASIA IN CONSTITUTIONAL DEAFNESS
(Compared with Cranial Dysplasia in Atrophic Rhinitis)

	Atrophic rhinitis		*Constitutional deafness*	
FEMALES				
Total cases	45		94	
	percentage		*percentage*	
Normal crania	10.3		6.8	
Type I "	9.1	20.5	9.2	27.7
Type II "	11.4		18.5	
Type III "	15.9	72.7	6.0	62.0
Type IV "	43.2		25.0	
Type V "	13.6		31.0	
Showing "sclerosis" ..	68.2		74.5	
MALES				
Total cases	24		59	
	percentage		*percentage*	
Normal crania	16.6		33.3	
Type I "	29.2	37.6	32.0	40.7
Type II "	8.4		8.7	
Type III "	33.3	45.8	7.2	26.0
Type IV "	12.5		7.2	
Type V "	0.0		11.6	
Showing "sclerosis" ..	20.9		27.5	

Calvarial sclerosis is an indication of constitutional inferiority; in both diseases almost three-quarters of the women give evidence of it, with the difference that in atrophic rhinitis the face is more apt to be inadequately grown in proportion to the brain-case, while in constitutional deafness the calvarium is more apt to be affected by a degenerative structural change.

There are, however, in both groups a significant number of women who show evidence of pituitary hyperfunction in the years of growth, and this is slightly more apt to be the case in constitutional deafness than in atrophic rhinitis. This fact precludes the view that the constitutional background is a purely hypofunctional state; it is more correct to regard it as dysfunctional.

In the males (Table I) this statement is still more justified, for in both diseases about 40 per cent show an instability on the hyperfunctional side. It appears, in constitutional deafness, that the male cranium shows less evidence of the constitutional disturbance than the female, since this group contains twice as many normal crania as the group with atrophic rhinitis. That the male face does not suffer to any great extent either in growth or in the degree of its differentiation in constitutional deafness is clear from the fact that types II, III and IV show relatively small occurrence. In both diseases the tendency towards sclerosis, indicative of degenerative change, is much less marked than in the females. This conforms with a finding in other groups studied, that pituitary stability is greater in the male than in the female; that, while the dyspituitary female tends to move towards the hypofunctional level, the tendency to hyperfunction is found more in the males.

Study of the cranial skiagrams of both sexes in the two diseases shows evidence of a constitutional background which is to be regarded as dyspituitary; that in the females the tendency is towards an earlier or later *hypo*function with a significant number presenting an earlier *hyper*functional phase. In atrophic rhinitis the facial part of the skull suffers to a degree not found in constitutional deafness, and this fact is more clearly evident in the males in whom normally the face undergoes a higher degree of differentiation than in the females.

The view that the constitutional background in progressive deafness is related to that of atrophic rhinitis is further strengthened by a second item of evidence, namely, that of a total of some 250 patients suffering from one or other of the two diseases we have found 42 cases in whom both defects are present. Thirty of these are females whose average age is 27 years, the youngest being 8 years of age and the oldest 55 years. The average hearing loss in the better ear is 27 per cent, while in the worse ear it is 36 per cent. In the male cases, which are 12 in number, the average age is 24 years, the youngest patient being 8 and the oldest 59; the average loss in the better ear is 28 per cent, while in the worse ear the loss is 34 per cent. It would appear that the association of these two constitutional diseases is more common than hitherto has been recognized.

Not only may the two defects be found in the same individual but in one generation of the family one defect may be found in certain members, while others have the second defect; and, further, not only may the two defects be distributed as it were horizontally in one genera-

tion of the family, but there may be a vertical distribution in succeeding generations. We have found a grandfather suffering from otosclerosis while his grandson shows the presence of atrophic rhinitis and, so far, no hearing defect, and this is in a family of excellent socio-economic status.

A third item of evidence suggestive of community of background in the two diseases is to be found in the response of a group of cases of constitutional deafness when an adequate number are treated for a sufficient length of time by a treatment which is directed specifically to the condition of atrophic rhinitis.

Of the cases treated between July, 1936, and September, 1938, there are 39 females and 16 males whose records are adequate from the point of view of this study. They were "run of the mine" clinic cases, and were mostly diagnosed as either "otosclerosis" or "nerve deafness"; no attempt was made to select any given type of case. In age they range from the second to the sixth decade of life. Treatment consisted of daily nasal insufflation of 1 c.c. of oil containing 1,000 international units of œstrin; other methods of administration have not yet been studied. None of the patients were treated for any period less than three months. Many of them have been under treatment for six months, and there are some who have been on treatment intermittently during the two years. As control over the same period 8 males and 6 females have been observed. Originally, an equal number of cases had been selected as controls, but it is hard to get regular attendance for examination purposes over long periods from patients from whom treatment is withheld.

Before and during the treatment, at intervals of from one to two months, the hearing acuity in each ear was measured with a standard Northern Electric 2 "A" audiometer in one of the clinic's ante-rooms which was quieter than the main clinic rooms, but was by no means a sound-proof room or even a quiet room. The tests were done by three well trained technicians.

It is freely admitted that the experimental

TABLE II.

TREATED MALES—HEARING CHANGE

Cycles:	*64*		*128*		*256*		*512*		*1,024*		*2,048*		*4,096*		*8,192*	
Case No.	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
1.....	**20**	**40**	**5**	**10**	**5**	**25**	**15**	**10**	**15**	**15**	**5**	**10**	**5**	**10**	**25**	–
2.....	–	**10**	5	–	5	10	5	–	5	–	5	5	5	5	25	–
3.....	–	5	–	15	–	5	**5**	**15**	**15**	**25**	–	**20**	**20**	**20**	**20**	**20**
4.....	15	10	15	5	5	–	10	5	–	5	**15**	**5**	**5**	**10**	**10**	**15**
5.....	**5**	**5**	**10**	**5**	**10**	–	**15**	**5**	**15**	**10**	**15**	**15**	**20**	**25**	35	–
6.....	**5**	**10**	5	5	10	–	5	5	5	5	–	5	**10**	**10**	–	5
7.....	5	40	–	5	**5**	**10**	–	5	–	5	5	–	–	–	–	5
8.....	**5**	**15**	10	5	**5**	**5**	**15**	–	**5**	**5**	**15**	**15**	10	**15**	15	–
9.....	–	–	–	–	5	–	–	–	–	–	10	–	15	10	10	15
10.....	**5**	**15**	–	15	–	15	–	10	**5**	**10**	–	–	**5**	**10**	**5**	**10**
11.....	**15**	**25**	**15**	**15**	**5**	**10**	**10**	**5**	**10**	**20**	**5**	**10**	10	**10**	10	**5**
12.....	**10**	**5**	–	5	–	5	5	5	5	5	**5**	**10**	–	–	**10**	**5**
13.....	–	5	5	15	5	5	10	5	20	15	25	–	10	5	**30**	**10**
14.....	**5**	**5**	**10**	**5**	**10**	–	**15**	**5**	**15**	**10**	**15**	**15**	**20**	**25**	35	–
15.....	10	–	10	5	10	–	5	–	–	**10**	**5**	**25**	**10**	**30**	**5**	**5**
16.....	–	**10**	**25**	**15**	**5**	**10**	**5**	**15**	**5**	**20**	**5**	**10**	–	**20**	–	10

UNTREATED MALES—HEARING CHANGE

Cycles:	*64*		*128*		*256*		*512*		*1,024*		*2,048*		*4,096*		*8,192*	
Case No.	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
1.....	–	–	5	10	–	–	10	5	5	15	10	15	5	–	5	5
2.....	–	10	–	5	–	10	–	10	5	20	5	15	5	30	–	25
3.....	5	–	–	5	5	–	–	–	–	–	5	15	15	–	–	–
4.....	10	–	10	5	10	–	5	–	–	**10**	**5**	**25**	**10**	**30**	**5**	**5**
5.....	5	**25**	15	**20**	20	5	25	–	20	5	25	5	20	5	–	5
6.....	–	10	5	10	10	15	10	5	10	10	5	–	20	25	30	–
7.....	**5**	**10**	**5**	**5**	5	5	–	5	–	5	5	5	–	5	15	5
8.....	5	**10**	10	5	–	–	–	–	–	5	–	5	5	5	5	–

Figures in bold face type signify sensation units improvement.
Plain figures signify retrogression.
– Signifies no change.

conditions were far from satisfactory during this period. It will be seen, however, from an account given elsewhere in this issue (p. 22) that much has been done to improve not only the general conditions under which the investigation is conducted, but also to render the method of testing in the current work not only more accurate but also more objective. Nevertheless, it clearly appears from the results of this preliminary, although imperfect, study that in certain cases of constitutional deafness intranasal œstrogenic treatment may produce very beneficial effects.

In Tables II and III is given a summary of the results of treatment in the cases of this series. The figures show the difference in sensation units for each ear for the various frequencies between the first and last audiograms of the period.

TABLE III.

TREATED FEMALES—HEARING CHANGE

Cycles:	*64*		*128*		*256*		*512*		*1,024*		*2,048*		*4,096*		*8,192*	
Case No.	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
1.....	**20**	**10**	**20**	**10**	–	–	**15**	–	**15**	–	**15**	–	**35**	**10**	–	**20**
2.....	**8**	**15**	–	**5**	**5**	–	**12**	**6**	**7**	**4**	**25**	**15**	–	**5**	**20**	**5**
3.....	–	**5**	–	**5**	**10**	–	**5**	–	**5**	**10**	**15**	**15**	**5**	**10**	–	**10***
4.....	–	**5**	**10**	**5**	**20**	**5**	**10**	**15**	**10**	**15**	–	–	**10**	–	**5**	–
5.....	**5**	**25**	**5**	**20**	**15**	**20**	**10**	**30**	**5**	**25**	**5**	**20**	**5**	**20**	–	–*
6.....	–	–	**15**	**15**	**5**	**10**	–	**5**	**5**	–	–	–	–	–	–	–
7.....	–	–	**5**	–	–	**5**	–	**10**	–	**5**	–	**5**	**5**	–	–	–
8.....	**15**	**10**	**10**	**10**	**15**	**5**	**10**	–	**5**	–	–	–	**5**	**15**	**5**	**20**
9.....	?	**15**	?	**10**	?	**25**	?	**25**	?	**35**	?	**5**	–	?	–	–
10.....	–	**15**	**10**	**10**	**5**	**5**	**5**	**5**	**5**	–	–	–	**5**	–	**15**	–
11.....	–	**25**	–	**20**	–	**15**	–	**5**	**10**	**10**	–	–	–	**10**	–	**5**
12.....	–	–	–	**5**	**5**	**5**	**5**	**5**	–	**5**	**10**	**5**	–	**15**	–	–
13.....	**10**	**15**	**5**	**10**	**5**	**15**	**5**	**20**	**5**	**5**	**5**	**15**	–	**10**	**10**	**25**
14.....	**15**	–	**15**	**5**	**5**	–	**10**	**5**	**5**	–	–	**10**	**5**	**5**	**10**	**5**
15.....	**10**	**25**	**10**	**30**	**25**	**30**	**25**	**30**	**40**	**45**	**45**	**40**	**50**	**45**	–	**20***
16.....	–	–	**5**	**5**	–	**10**	–	**5**	–	**5**	**10**	–	–	**5**	**5**	–
17.....	**5**	**5**	**10**	**10**	**10**	**10**	**5**	–	**5**	–	–	**5**	**5**	**5**	**5**	**5**
18.....	–	–	–	–	**5**	–	**5**	**5**	–	**5**	**10**	**10**	–	**10**	**5**	–
19.....	–	**5**	–	**15**	**10**	**5**	**5**	**5**	**10**	**5**	**5**	**10**	–	–	**15**	–*
20.....	–	**5**	**5**	**5**	–	**5**	**5**	–	**5**	**5**	**10**	**10**	–	**10**	**5**	**10**
21.....	**5**	–	**5**	–	–	–	–	**5**	–	**5**	**5**	**5**	–	–	–	–
22.....	**35**	**15**	**25**	**25**	**60**	**35**	**40**	**15**	**55**	**25**	**30**	**10**	**35**	**15**	**35**	**20**
23.....	**25**	**20**	**40**	**30**	**35**	**25**	**30**	**15**	**30**	**5**	**10**	–	–	**25**	**30**	–*
24.....	**5**	**5**	–	**5**	**5**	**5**	–	**10**	–	–	**10**	**5**	–	–	–	**5***
25.....	–	**10**	–	**5**	–	**5**	**5**	–	–	–	**5**	–	–	–	–	**15**
26.....	**10**	**15**	**5**	**15**	**5**	**5**	**40**	–	**25**	**10**	–	–	–	–	–	–*
27.....	**15**	**5**	**10**	**10**	–	**5**	**15**	**10**	**35**	**10**	**40**	**15**	**35**	**25**	**30**	**10***
28.....	–	**15**	**5**	**5**	**15**	**5**	**5**	–	**5**	**5**	–	**5**	–	**5**	–	–*
29.....	**15**	–	**5**	–	**5**	–	**5**	**5**	**5**	**5**	**30**	**5**	**5**	–	**10**	–
30.....	**10**	–	**5**	**5**	**5**	**5**	**5**	–	**5**	–	**10**	**5**	**15**	**15**	**10**	**10***
31.....	**10**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**10**	–	**20**	–	–	–	–
32.....	**10**	**10**	**10**	–	**10**	**5**	–	**5**	–	**5**	–	**5**	–	**5**	**5**	**5**
33.....	**5**	–	–	–	**5**	–	**5**	**5**	**5**	**5**	**5**	**10**	–	–	**5**	–
34.....	**5**	**5**	**5**	–	**10**	**5**	**5**	–	**10**	**5**	**25**	**20**	**10**	**10**	–	–
35.....	**30**	**5**	**20**	**5**	**5**	**5**	**10**	–	**5**	–	**5**	–	**5**	**5**	**10**	**15**
36.....	**10**	**5**	**20**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	–	–	**5**	**15**	**15**
37.....	**5**	–	**5**	**5**	**5**	**5**	**5**	–	**5**	**10**	**5**	**5**	–	**5**	**15**	–*
38.....	**10**	**20**	**5**	**15**	**15**	**25**	**5**	**5**	**5**	–	**5**	**10**	**10**	**5**	–	**35?**
39.....	**5**	**10**	**5**	**10**	**10**	**10**	**5**	**10**	**10**	**10**	**10**	**10**	**5**	**5**	**10**	**5**

UNTREATED FEMALES—HEARING CHANGE

Cycles:	*64*		*128*		*256*		*512*		*1,024*		*2,048*		*4,096*		*8,192*	
Case No.	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
1.....	**5**	**10**	**5**	–	–	**10**	**5**	–	**5**	**15**	**5**	**5**	**25**	–	?	?
2.....	–	**5**	**5**	–	**5**	–	–	–	**5**	**5**	**20**	**10**	**5**	**15**	**5**	**5**
3.....	–	–	**5**	**10**	**5**	**5**	–	–	–	–	**5**	**5**	**5**	–	**5**	–
4.....	**5**	**5**	–	–	**5**	**5**	**15**	**5**	**5**	**5**	**15**	**10**	–	**10**	–	**40?**
5.....	**5**	**5**	**10**	–	**5**	–	–	**10**	–	–	**5**	**5**	–	–	**5**	**15**
6.....	**10**	**5**	–	**5**	**10**	**5**	**5**	**5**	–	–	–	**5**	**5**	**5**	–	–

Figures in bold face type signify sensation units improvement.
Plain figures signify retrogression.
– Signifies no change.
* Signifies marked improvement in tinnitus.

Bold-face figures show improvement, light figures show retrogression, while a dash indicates no change.

It is of course useless to compare individual cases with others in their group, either from the point of view of diagnosis, severity of condition, or response to treatment, except in the broadest way. It is, however, useful to compare the treated group as a whole with the untreated group by statistical examination of the audiometric data given in Tables II and III.

Statistical examination shows that when all the data for 512, 1,024, 2,048, and 4,096 cycles are considered, the treated males do on the average improve slightly in hearing, while the untreated males slightly deteriorate. The average improvement and the average deterioration are highly significant, statistically. At these same frequencies, it is also possible to assert that the treated females do on the average improve slightly in hearing. The untreated females appear to deteriorate, and it is likely, *a priori*, that they should do so (as the males undoubtedly do); but the number of untreated females studied is too small to allow one to assert that their apparent deterioration is a real one and statistically significant; it is possible, though improbable, that untreated females in a large series would be found to improve as much as the treated females do. This would seem to indicate that, however far recession may seem to have occurred in man's ontogenetic development from an earlier and closer "oto-genital" relationship in phylogeny, sex hormone may still play a rôle in the physiology of hearing today in modern man, at least when constitutional defective function exists.

SUMMARY

1. The results of the empirical use of intranasal œstrin insufflation in a series of 55 cases of constitutional deafness are reported.

2. The high frequency of occurrence of cranial dysplasia in a series of 153 cases of constitutional deafness is also reported.

3. Attention is drawn to the distribution of cranial types in this group and its similarity to the type distribution already reported in a series of cases of atrophic rhinitis and ozæna. It is suggested that these two constitutional diseases may have a similar or even share a common constitutional background.

4. This view appears to find additional support from two clinical facts herein reported. First, it is shown that the two constitutional defects coexist in the same individual and in the same familial stock more often than has hitherto been recognized. In such stock the two defects may be distributed through one generation or in successive generations. Second, it is shown that treatment which acts specifically upon the nasal disease is capable of producing not only marked improvement in certain individual cases of the aural defect but also a statistically significant amelioration in the hearing level of a group of constitutionally deaf as a whole.

5. It is not suggested that constitutional deafness is an endocrine disease.

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At the end of 1936 there were in Canada 43,080 persons registered in the fifty-seven institutions for the care and treatment of persons suffering from mental diseases, of whom 39,833 were resident patients and 3,247 on parole. The net increase in resident population during the year was 1,562. The total number of patients under care was 53,326—an increase of 2,592 patients over the number under care in 1935. Of the 39,833 patients in residence, 31,268 were classified as insane, 7,711 mental defectives, 603 epileptics, and 251 all other types. The ratio of insane resident patients per 100,000 of the mean general population at the end of December, 1936, was 282.2, and for the total resident patients 359.5. First admissions numbered 9,002, or 74.4 per cent of the total, and readmissions 2,121, or 17.5 per cent of the total. Of the first admissions, 5,443, or 71.7 per cent, were Canadian born, 1,021, or 13.4 per cent, were British born, and 1,128, or 14.8 per cent, were foreign born. The staffs of all mental institutions numbered 7,538 and the total expenditure during the year was $14,222,138.

IMPROVEMENTS IN AUDIOMETRY AT THE MONTREAL GENERAL HOSPITAL*

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Montreal

THE researches being pursued by members of the staffs of the Department of Biochemistry, McGill University, and of the Ear, Nose and Throat Department of the Montreal General Hospital required reliable tests of the threshold of hearing of cases investigated, in order that changes of the deafened threshold might be detected if such occurred from time to time.

Since the changes of loss of hearing rather than the loss of hearing itself are of particular importance, direct reference of intensity measurements to the same stated power level would be more convenient than the conventional reference to the level of the threshold of hearing of the normal subject at each frequency, and a high precision test technique must be applied. Given sufficiently precise measuring apparatus, the recorded results of tests could still be largely affected by (1) the method of the application of the stimulus; (2) the reliability of the subject's response; (3) the control by the technician and the recording of observations.

The method of application of the stimulus.— The most obvious opportunity for error in applying an auditory stimulus by means of earphones would be that due to masking of the sound in the ear by leakage from the room to the ear tested past the earphone in case the noise level in the room were appreciable. This effect is relative and with considerably deafened thresholds the noise level would have to be high to cause error. Such high levels of noise did occur in the rooms of the Clinic, and it was felt essential that a quiet room should be provided to reduce this source of error.

Another question considered was the extent to which direct vibration from the earphone reaching the ear by bone conduction instead of by the air column may affect the result. Such an effect might be greater with the higher stimulus intensities required at the threshold for deaf patients than for tests of subjects with normal hearing, and yet might not be directly proportional to the intensity. Under this circumstance it seemed logical to provide a room so fully sound-proof that the noise level would be below the threshold of normal subjects, thus eliminating this source of error in all cases including routine tests employing audiometers of conventional design; but at the same time the other possibility of error could be eliminated if the patient were placed without earphones in an open sound field such as could be produced at a convenient distance from a loud speaker. Further to simulate the naturalness of the conditions the subject could be placed facing the source of sound at about the same distance as one would naturally face the speaker in ordinary conversation. A sound-proof room has been built and is described in the appendix.

It was also decided to provide an equipment for open sound-field testing which differs from a 2A audiometer in the use of a loud-speaker instead of the earphones and in using a constant reference level of intensity for all frequencies. It otherwise uses similar electrical apparatus but of much larger power capacity, higher precision, and of wider frequency, range and scope. It generates either a pure tone as in the 2A audiometer or, alternatively, a so-called "warble tone". This is a tonal effect produced by varying the frequency over a small range about the mean frequency, the time of a complete cycle of this variation being one-thirtieth of a second. This "warble" has quite a different quality from a pure tone, is more readily recognized by the subject, reduces fatigue, and reduces the effect of standing waves in the sound-field.

A chair with an adjustable head-rest is placed in front of the loud-speaker so that the line through the ears of the subject intersects the speaker axis, one meter from it. The speaker axis is on the diagonal of the sound-proof room which was constructed with inside dimensions of approximately a ten-foot cube. The apparatus is installed in an anteroom, and the subject is observed through a convenient window by the operator seated at the audiometer controls. Fig. 1 shows the view through this window.

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In this sound-proof room tests are made both with a 2A audiometer and with the open sound-field audiometer, the former being used for routine tests and the latter for selected cases, usually over a selected and restricted frequency range. The Governors of the Montreal General Hospital have provided these improved facilities.

The reliability of the subject's response.—The majority of patients have had no previous experience of audiometer tests and it was considered specially important that methods should be employed which would reduce to a minimum the effect of conditioning of the patient by re-test at intervals during treatment. Otherwise, later tests might show an improvement of hearing actually due to a better understanding by the patient of the test requirement, but which might be erroneously attributed to treatment. For this purpose a technique involving successive trials by stimuli selected at random in the neighbourhood of the threshold was adopted. This generally speaking follows the method employed in the Bell Telephone Laboratories for measurements of loudness.[1]

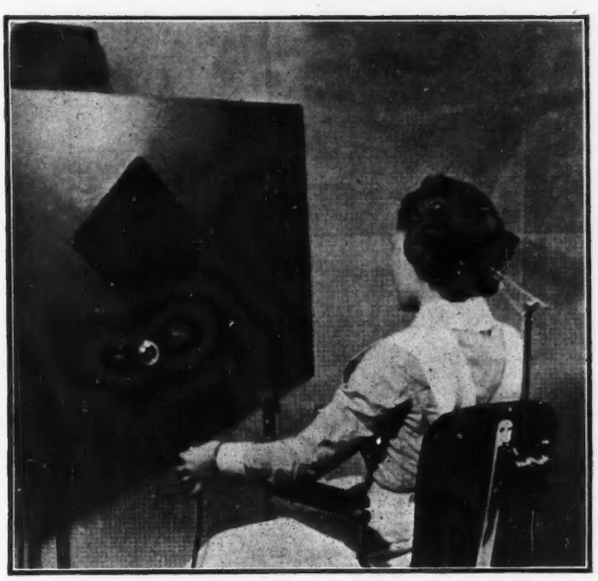

Fig. 1.—The field of view from the observation window. Audiometric room, Montreal General Hospital.

The method is as follows for a threshold test at any stated frequency. Each of a number of sound intensities, differing by an equal amount, and covering a range of intensity within which the threshold is known to lie, are introduced to the subject the same number of times. A zero stimulus is presented once. The order of presentation should be as near as possible random, that is to say this order will be determined only by chance.

Some of these sounds will certainly be audible to the patient; others will be inaudible. The patient is required to signal "yes" or "no" by pressing the proper push button in reply to a signal which lights a lamp beneath the loud-speaker when the tone is presented. He has no guide to this decision other than his own sensation of hearing, since the intensity presented to him in any particular trial is a matter of chance, and he is merely informed by the lighting of the lamp that a trial is in progress.

Since the range covered by these trials extends from intensities heard with certainty to intensities which just as certainly are not heard, between these extremes lies a point of complete uncertainty. At this point of complete uncertainty the patient's decision between the two alternatives offered to him must follow the laws of chance, and, given a sufficient number of trials, he would reply "yes" to 50 per cent of the number of trials. This point is taken as the "threshold of hearing". With a moderate number of trials it may be found with reasonable accuracy by plotting the percentage "affirmative response" curve on a sound intensity base. The 50 per cent response point of the curve is by definition the "threshold of hearing". Sufficient accuracy is obtainable if the curve be plotted for six intensities, each presented five times to the patient, which, with the zero, stimulus trial, is thirty-one trials for a single test.

Such a method would be burdensome if manual operations were required for each trial, but a machine called "the random stimulus selector" is used to perform these actions after manually setting the audiometer so that the threshold is within its range. It performs the following actions. It mechanically selects at random one of the six intensities chosen or the zero intensity, and presents this to the patient, lighting a lamp to inform the patient that the trial is proceeding. A switch provides the choice of either 20 DB or 10 DB range covered by the six intensities. It counts the number of trials of each intensity and locks each out of use when the stated number of trials of that intensity is completed. These counters are adjustable from 1 to 10 trials, but 5 trials are generally used. Fig. 2 shows a record card with these curves drawn and the thresholds indicated. This is the record of replies to five trials of each of six sound-intensities at each frequency.

It is reasonable to suppose that conditioning of subjects by retesting at intervals during treatment would not affect their judgment in the range where affirmative or negative certainty exists, but would rather decrease the range of uncertainty. With conventional methods of threshold testing, using increasing or decreasing stimuli, this might result in a shift of the threshold value, but the effect by this method would be merely a steeper slope of the curve through the 50 per cent response point without change of threshold value. For this reason we believe the method to be well suited for use where precise threshold values obtained on the first occasion of test must be compared with values obtained later by retests at intervals of weeks or months.

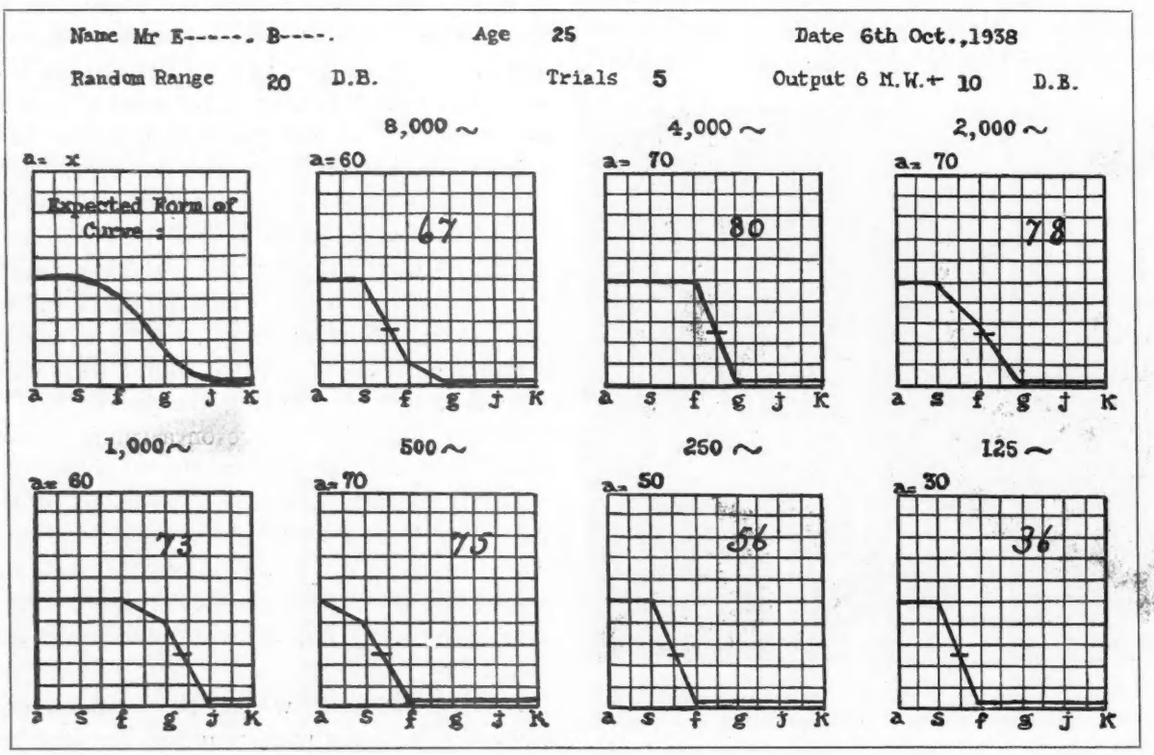

Fig. 2

Control by the technician and recording of observations.—It is quite possible for accurate tests to be made unreliable by errors in transcribing records, and for this reason a method was devised by which the patients' replies are automatically recorded on a card which forms without transcription part of the permanent record. This is done in the following manner.

Electric solenoid operating mechanisms were provided for eight keys of a standard typewriter. When the patient presses the "no" button a semi-colon is typed. When he presses the "yes" button an "asterisk" is typed if the zero stimulus was then presented to the patient; and one of the letters a, s, f, g, j, or k, according to which of the six differing sound intensities was then presented to the patient. Each letter typed on the card then signifies an affirmative reply by the patient to a trial of a specific sound intensity. The letter "a" is the strongest sound and the others represent weaker sounds of equal decrements in the order stated by step of 4 or 2 DB. As all sounds have been introduced the same number of times a simple count of the number of times each letter appears will give the fraction of affirmative response to each sound intensity.

Table I shows a card recording the results of such a test and the count of these letters is the means by which the curves in Fig. 2 were drawn. While the record card is in the typewriter the technician types in by hand the data indicated to complete the record. The electrical operating mechanism does not in any way interfere with the manual use of the typewriter.

The apparatus is so arranged that after the patient has pressed one or other of the reply buttons he is unable to alter the course of events which is in the following sequence. The typing of the reply is immediately followed by de-energizing of the "random stimulus selector"

TABLE I

Name Mr. E-. B-. Age 25 Date Oct. 6, 1938 Random Range 20 D.B. Trials 5 Output 6 M.W. +10 D.B.			
Freq.	*"a"*	*Record*	*Thd.*
16,000			
8,000	60	(a;;sss;a;;;;;;;;;ss;;f;;;;;;;aaa)	67
4,000	70	(;fasffsf;s;s;f;;;;;;;;aa;;;sss;;)	80
2,000	70	(;fa;as;;;;a;;fa;a;s;ss;;;;f;;;s)	78
1,000	60	(af;aa;;a;;;ffs;;asgfs;fs;s;gg;g)	73
500	70	(;s;a;;;a;;;;;;;sa;s;a;as;;;;;;;;)	75
250	50	(;aa;;aasas;ss;s;;;;;;;;;;;;;;;;)	56
125	30	(;s;;;aa;;;;;;;s;;;a;;a;ass;s;;;;)	36

The letters under "Record" are supposed to be typewritten letters.

which terminates that particular trial. After an interval of about five seconds automatic re-energizing of the random selector takes place, starting a new trial. The technician manually begins a test by closing a switch after preliminary settings and adjustments have been made. Everything is then automatic, except that the patient may press either the "yes" or "no" button when he has made up his mind what reply he will give. In either case that action ends the trial and initiates the next trial. When all trials are complete a lamp notifies the technician that the test is over. He then manually opens the switch and resets the apparatus for the next test. The time of test for five trials of each intensity varies with the quickness of the patient, but generally is from four to five minutes.

The technician is required to record accurately on the card the audiometer power level, the numerical value of "a", and the random range, by reading the dials of the audiometer. During the actual test he has at least four minutes during which he can verify these values and with reasonable care this card record should be very reliable.*

We believe that the combination of the mechanical random stimulus selection over a range within which the threshold lies and the automatic recording on a permanent case-record card precludes the most likely causes of error in the threshold of hearing testing with unskilled subjects. We are led to believe that with subjects of ordinary intelligence first tests of threshold by this equipment may be obtained with practically equal precision as in later tests. A re-test within an hour on a new subject has been undertaken on several occasions and agreement found consistent with published data on the least perceptible change of intensity at the threshold of a normal subject.[2] In many cases, even of very deaf people, the range of indecision of new subjects is found to be as narrow as with quite skilled subjects of normal hearing. This might be expected if the subject had a "variable" type of deafness.[3] As a result of the rate of change of loudness, for a small increment of intensity just above the threshold, being greater for "variably" deaf people than for normal subjects; the range of uncertainty, other things being equal, should be less.

This type of installation is also applicable to other fields of investigation, such as comparison of the threshold with and without hearing aid, and comparisons of levels at which articulation is clear.

APPENDIX

The sound-proof chamber (see Fig. 3).—The exclusion of air-borne sound was the first condition of providing the high degree of sound-proofing desired, and in consequence the chamber with its doors and windows must be practically air-tight. Any attempt to provide artificial ventilation during tests would involve problems which seemed practically insoluble at reasonable cost, and consequently the air-volume must be sufficient for fairly long tests without replenishment, except that a powerful fan could be used to change the air at convenient intervals between tests. Also it was desirable that the dimensions should be sufficient to overcome any likelihood of producing symptoms of claustrophobia in the subjects tested. Inside dimensions of a ten-foot cube were chosen to meet these requirements. The cubical form has the advantage of providing the minimum surface area for sound transmission of any rectangular form of the required volume, and, consequently, the quantity of materials of construction used would be a minimum.

This chamber was constructed with a reinforced concrete floor slab, four inch brick walls, and a reinforced concrete ceiling slab, providing a chamber of sufficient structural strength and moderate weight. One small window opening

* The random stimulus selector and recorder were designed and constructed by one of the authors (E.G.B.) for the Department of Biochemistry, McGill University, out of research funds provided by the American Otological Society.

and one door are provided. The window opening is closed by three-eighth inch plate glass, not mounted in a sash but clamped against a steel frame which is embedded in the brick work. A rubber gasket is used to make the joint air-tight. The door opening has similarly a steel frame embedded in the brickwork, and a steel-plate door, properly braced and lined with vibration-damping material, closes against the frame with a rubber gasket to make the joint air-tight under the action of clamp-type latches such as are used for refrigerator doors. In this manner the openings are sealed air-tight by materials of high density. The chamber so constructed reduces to a minimum the access of sound by air-conduction, and, owing to its rigidity and the high density of the materials of which it is constructed, would reflect a very large part of the sound-energy incident on it if it were isolated in a sound-field in air. This condition is simulated by suspending it within another chamber by a tension rod at each corner, using damped springs at the four points of support.

The outer chamber is of heavy concrete construction, and the corresponding window and door openings are similarly sealed. It is partly above ground level and partly within an earth embankment. It is carried on a foundation separate from the main hospital building, partly on a pipe tunnel, and the junctions of the walls with the hospital walls are not banded but caulked with a waterproofing material to reduce the transmission of machinery noises from the main building walls, as far as practicable. Tests made with an electric stethoscope showed a rather high level of noise in the building walls at this point, with a vibration at about 100 cycles per second predominating. Noise in the tunnel walls at the point of support was of negligible amount.

With these precautions taken, the structure of the outer chamber would be fairly free from noise conducted from other structures, and its massive and air-tight construction would reduce to a small value the transmission of traffic noises. The rate of transmission of sound energy into the air space between the inner and outer chambers would then be very low, and the inner chamber would reflect a very large amount of such energy. To reduce the build-up of the energy level in this air-space consequent on interreflection between the surfaces of the inner and outer chambers, sound-absorbing material was provided in this space, consisting of a two-inch layer of loose mineral wool above the ceiling and below the floor and a blanket of mineral wool, one inch thick, supported in a wire-mesh

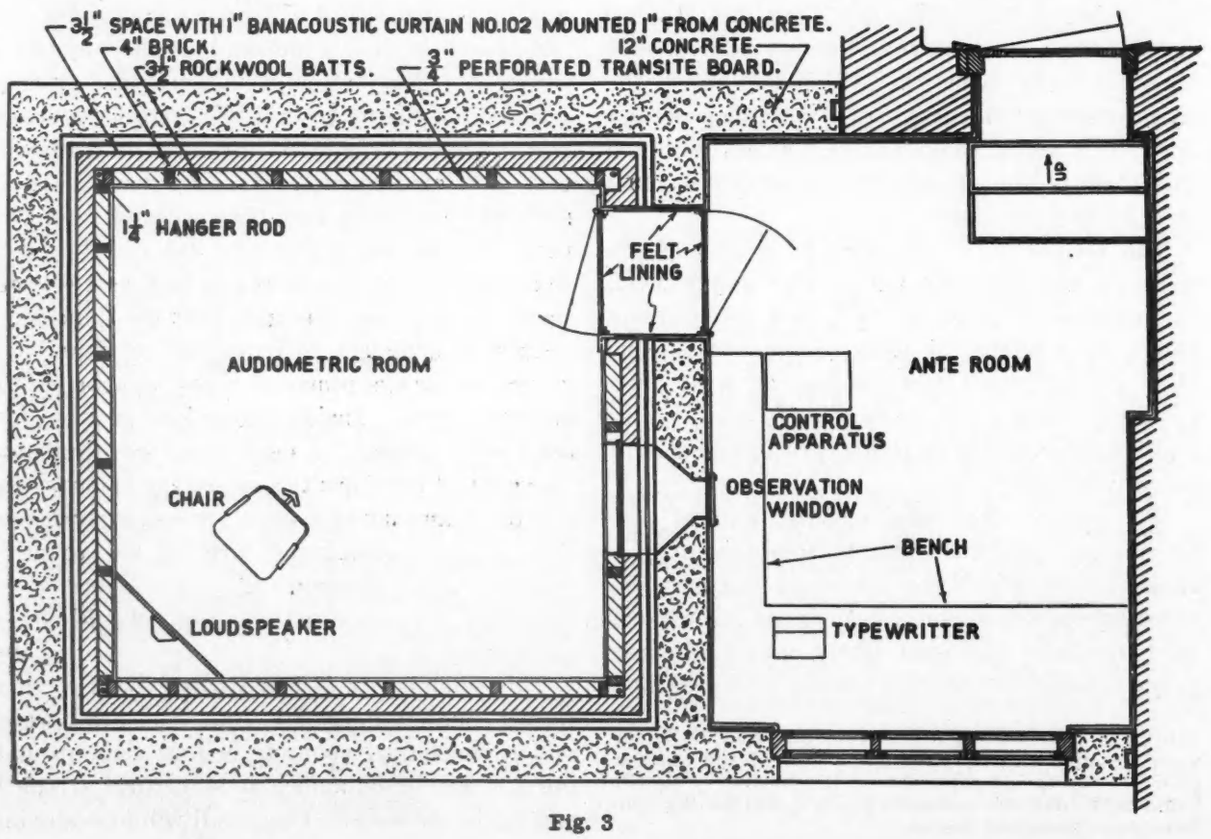

Fig. 3

net and fastened to the inside of the walls of the outer chamber at a distance of one inch therefrom by nailing strips of wood on these walls.

This air-space is only 3½ inches and was kept small for reasons of economy, as the amount of material used for the outer chamber increases rapidly with an increase of this dimension. This space is not bridged by solid material anywhere except the four suspension springs. The door sill has a flexible support, and closure at the door and window to preserve neatness is effected by a fabric lining.

The inner chamber has an acoustic lining to reduce sound reflections and the standing waves consequent thereon. It consists of mineral wool "batts", four inches thick, stacked between wood "studs" on the walls and ceiling, and supported by galvanized wire mesh nailed to the studs. The whole is covered by perforated "transite" panels screwed to the studs with wooden spacing straps, to maintain the panels clear of the face of the mineral wool lining. This provides a neat washable wall and ceiling surface.

The degree of sound-proofing accomplished is indicated by the fact that under ordinary conditions the keenest ear is unable to detect noise from the outside, that two persons could not agree whether or not they heard a very loud motor horn blown within a foot of the wall of the building, but the sound of a hammer and chisel applied to the main building structure close to the sound-proof room is just audible within the chamber. This latter fact indicates the desirability of complete structural discontinuity between the enclosing chamber and other buildings, but in practical use it is easy to locate the source of such disturbances and stop them.

The architect was J. Cecil McDougall, Montreal. We are grateful to H. J. Vennes and other engineers of the Northern Electric Company for helpful criticism of earlier designs, and to Prof. H. E. Reilley, of McGill University, for suggestions in the matter of absorbing materials. We are especially indebted for the willing cooperation of the Governors of the Montreal General Hospital in bearing the expense of construction of the sound-proof room and for providing the greater part of the electrical equipment; also, to the Central Bureau of Research of the American Otological Society for grants in support of this work to Professor Collip in 1937 and 1938.

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A BIOCHEMICAL STUDY OF PATIENTS ON SULPHANILAMIDE THERAPY

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VARIOUS dosages have been used by members of the medical profession who have prescribed sulphanilamide. Some have preferred to use very large doses, while others have been more conservative and have prescribed doses so small that it is doubtful whether any benefit could be expected from such cautious measures. The experiments to be reported in this paper were performed in the hope that with the aid of the data obtained sulphanilamide therapy might be applied more intelligently. This work is part of a study of the use of sulphanilamide in urology which is being conducted by the authors, with the collaboration of Dr. P. H. Greey, of the Department of Pathology and Bacteriology. The present communication describes some of the biochemical studies, both academic and clinical, which have served as a foundation for the clinical work which will be reported shortly.

These studies fall naturally into three sections: (1) the response of persons with normal kidney function to single and multiple doses of sulphanilamide; (2) the response of patients with more or less impairment of kidney function to similar procedures; (3) the response of patients to various dosage regimens which have been used clinically.

I. THE RESPONSE TO SINGLE AND MULTIPLE DOSES (NORMAL KIDNEY FUNCTION)

Patient B. was a male, aged 33, weighing 165 lbs., suffering from urethritis and cystitis, both specific and non-specific. This condition had been present for ap-

proximately eight months when the experiments described below were begun. He had been seen some months earlier and was put on routine sulphanilamide therapy, but had disappeared from the clinic for about six months. When he returned, with the condition unimproved, it was discovered that he had continued to take the drug of his own volition throughout this period. It was estimated that he had ingested about 7,500 grains (over a pound) of the drug. At this time hæmoglobin, differential white cell count, and kidney function were normal. In an effort to discover why he had not been cured, bacteriostatic tests were performed on the various organisms isolated from his urine. These indicated that the infecting organisms would not respond to sulphanilamide. He was later cured by routine irrigation treatment.

He was given 30 grains (1.947 or approximately 2 grams) of prontylin at 8.30 a.m.; blood samples and total urines were collected every 30 minutes for four hours, at 2 hour intervals for the next 8 hours, and then at 24 hour intervals for several days. Fluid intake was adjusted to produce about 2 litres of urine on the first day. The results of the analyses of these specimens are shown in Fig. 1.

The blood.—The maximum concentration of (free) sulphanilamide in the blood was reached in about four hours. The concentration of free sulphanilamide remained relatively constant (2.5 mg. per cent) for another four hours and then fell gradually, so that at the end of 24 hours slightly less than 1 mg. per cent remained. Conjugation of the drug was delayed in this particular instance. Maximum concentration of the conjugated drug in the blood was not obtained until four hours after the peak of free sulphanilamide had been reached. This is not the usual finding; generally the two maxima are simultaneous.

The urine.—Maximum concentration (45 mg. per cent) of free sulphanilamide was obtained in 3 to 4 hours. Following the noon meal the concentration fell to 13 mg. per cent, but it rose again until by 8.30 p.m. the value was once more 45 mg. per cent. The overnight urine contained 40 mg. per cent of free sulphanilamide.

Completeness of excretion.—During the first twenty-four hour period (urine volume, 1,915 c.c.), a total of 1.08 grams of sulphanilamide was excreted; during the second day (urine volume, 1,230 c.c.), another 0.49 grams were eliminated; on the third day the total urinary output (volume, 1,720 c.c.), was 0.17 grams; by the end of 72 hours 89 per cent had been excreted.

Conjugation of sulphanilamide.—The fraction in the conjugated form varied considerably. Up to the end of the first 2 hour period no conjugated sulphanilamide was found in the urine; during the next hour 28 per cent of the drug excreted was conjugated; at the end of 4 hours 33 per cent; at 8 hours 44 per cent; after 12 hours 50 per cent; and in the 12 to 24 hour urine 67 per cent was in the conjugated form. The average value for the conjugated fraction in the first 24 hour urine was 51 per cent of the total drug excreted, while in both the 24 to 48 and 48 to 72 hour urines it was 75 per cent.

The same patient, a week later, was given another 30 grain dose (2 grams) of sulphanilamide, but fluids were forced during the first 12 hours. It is interesting to note that absorption seems to have been more rapid in this second experiment (Fig. 2). The maximum concentration of sulphanilamide in the blood (4.0 mg. per cent in 2.5 hours) is both earlier and higher than in the first test dose (2.5 mg. per cent in 4 to 6 hours). The first 24 hour urine (volume, 5,130 c.c.) contained 1.05 grams of sulphanilamide, of which 46 per cent was conjugated. The urines were naturally much more dilute, but the total quantity of drug excreted and the percentage conjugated were almost the same as in the first experiment. The 24 to 48 hour urine (volume, 1,300 c.c.) contained 0.53 grams (74 per cent conjugated) and the 48 to 72 hour urine (volume, 1,920 c.c.) contained 0.13 grams (62 per cent conjugated). By the end of 72 hours 88 per cent of the dose had been excreted in the urine.

It should be noted that in this patient with normal kidney function the urinary output of sulphanilamide on a normal fluid intake (2 litres) and on an excessive fluid intake (5 litres) is practically the same. It has been claimed repeatedly by clinicians that patients developing toxic symptoms should be given increased quantities of fluids to accelerate the elimination of the drug. This patient, with normally functioning kidneys, did not respond in the expected manner. Increased fluid intake possibly may be effective, however, in accelerating the elimination of the accumulated drug in patients with some forms of kidney damage. We have not considered it advisable to deliberately conduct such an experiment upon patients with impaired renal function, and fortunately no occasion has arisen which necessitated such a procedure.

Over a week later this patient was given repeated 30 grain doses in an attempt to raise the blood concentration to a higher level. The drug was given at 8 a.m., 10 a.m., 12 noon and 8 p.m. —*i.e.*, 120 grains in 12 hours. At 8 a.m., 2 p.m., and 8 p.m., on the following day, he received

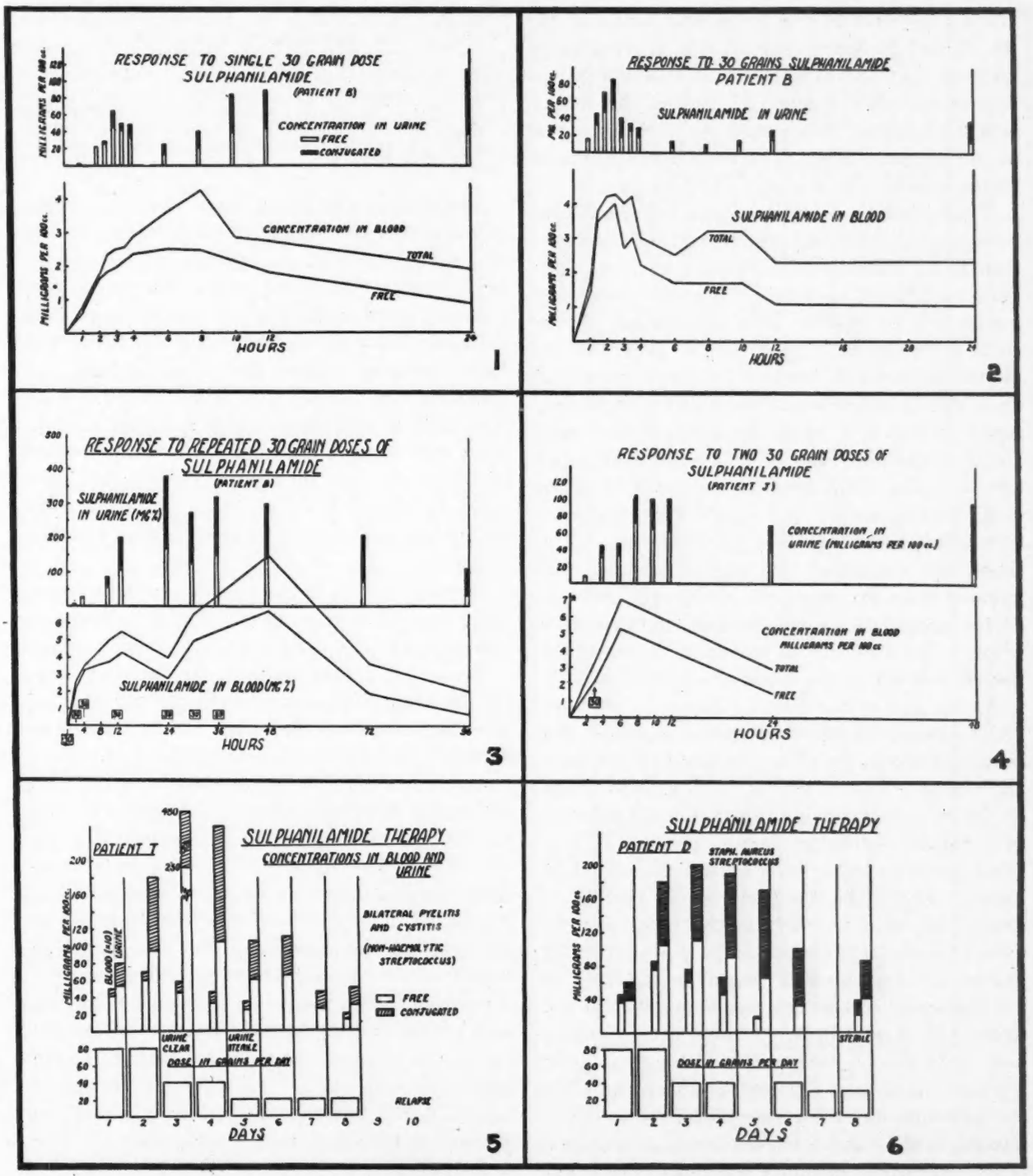


Fig. 1.—Biochemical response with normal fluid intake. **Fig. 2.**—Same person (as in Fig. 1); fluids forced during first 12 hours. Note earlier and higher peak in blood curve than in Fig. 1. **Fig. 3.**—Biochemical response of same person (as in Figs. 1 and 2) to repeated 30 grain doses of sulphanilamide. Note relatively low blood concentrations and high urine concentrations on first day. **Fig. 4.**—Biochemical response with slightly impaired kidney function. Note continued rise in blood curve to concentrations nearly double those following single dose. **Fig. 5.**—Biochemical response of patient with infection during therapy. Note marked increase in urinary concentration of drug on third day; apparently with elimination of the infection the excretory ability of the kidney was greatly improved. **Fig. 6.**—Biochemical response of patient with bilateral pyelitis to sulphanilamide. Columns have same significance as in Fig. 5, *i.e.*, the wide column gives urine concentration (clear portion = free, cross-hatched portion = conjugated), the narrow column is 10 times the blood concentration.

further 30 grain doses. Blood samples and total urines were collected at two hour intervals during the first twelve hours, and again at 24, 48, 72 and 96 hours (Fig. 3). It is remarkable to note that the blood concentrations were no higher during the first day (when the intake was 120 grains) than they were following a single 30 grain dose. The urine concentrations were, however, very high.

These findings confirm those reported previously (Lucas[1]) that with normal kidney function blood concentration above 4 to 5 mg. per cent is difficult to attain. Massive dosage or conditions interfering with elimination of the drug are necessary to achieve the generally accepted therapeutic level of 10 mg. per cent of free sulphanilamide in the blood. Referring again to Fig. 3, it would appear that the tissue fluids of the body had become nearly saturated by the end of 24 hours, for the three 30 grain doses on the second day caused the blood concentration to rise to 6.75 mg. per cent. The blood also contained 3.25 mg. of inactive conjugated drug, giving a total of 10.0 mg. per cent, at the end of 48 hours. No further doses were given. The rapidity of excretion is shown by the rate at which the blood concentration fell.

At the end of the first 24 hours 41 per cent (3.22 grams) of the 7.80 grams ingested had been excreted in the urine, leaving 4.58 grams in the tissues. The 90 grains (5.85 grams) taken on the second day would raise the total quantity in the body to 10.43 grams; 45 per cent of this (4.66 grams) was excreted during the second 24 hours. During the third day 54 per cent (3.11 grams) of what was left in the body was excreted, while on the 4th day 50 per cent (1.32 grams) of the drug still present in the body at the beginning of this day was eliminated in the urine. In other words, 60 hours after the last dose 12.31 grams (90 per cent of the total drug ingested) had been excreted in the urine. By the following day the concentration of sulphanilamide in the blood was very low (< 1 mg. per cent), but small amounts continued to be excreted in the urine for several days longer. More than 80 per cent of the drug excreted in the later periods was in the conjugated form.

II. The Response to Single and Multiple Doses (Impaired Kidney Function)

Patient J., male, aged 71 weight 125 lbs.; carcinoma of the prostate and cystitis. Non-protein nitrogen slightly elevated (45 to 54 mg. per cent); phthalein test, 81 per cent excreted in 2 hours; water test, a fair response; hæmoglobin 70 per cent.

Because of the presence of slight kidney damage (evidenced by function tests) caused by obstruction at the prostate, he was selected for comparison with patient B. At the time of the test the obstruction was relieved by an in-dwelling catheter. The patient was given a 30 grain dose of sulphanilamide; the blood and urine were collected as described above. The blood levels and urine concentrations were essentially the same as in the case of patient B. (maximum blood concentration 2.66 mg. per cent in 4 hours; maximum urine concentration 79 mg. per cent free, 86 mg. per cent total at 4 hours).

About a month later, when the non-protein nitrogen was 40, the same patient was given two 30 grain doses with an interval of 3 hours between them. Blood samples and total urine were collected as shown in Fig. 4. The concentration of sulphanilamide in the blood following the first dose was within the normal range, but following the second the blood concentration was doubled, which is not the finding in subjects with good kidney function. Elimination of sulphanilamide by the kidney was not seriously impaired, however, since the blood concentrations returned to reasonable levels within 24 hours.

During the first 24 hour period (urine volume, 2,660 c.c.) 48 per cent of the total drug ingested was excreted. On the second day (urine volume, 2,120 c.c.) a similar amount was excreted; thus by the end of 48 hours about 98 per cent of the drug could be accounted for in the urine. Traces of sulphanilamide were still recoverable on the third day, the urine containing 2.5 mg. per cent free and 13 mg. per cent total. During the first two hour period no conjugated drug was detected in the urine. The fraction of conjugated sulphanilamide increased steadily until it reached 85 per cent of the total excreted in the urine on the second day and was about the same fraction of the total on the third day.

Because of our hesitation to experiment with patients showing evidence of more severe kidney damage no attempt was made to obtain complete data from such cases. The drug has been used clinically in a few patients of this type and the incomplete records obtained are presented later in the paper.

III. The Response to Accepted Clinical Procedures

Biochemical control of patients on various commonly employed dosage regimens has also been done. The routines which have been used in urology are of two general types: (1) large initial dosage, with subsequent decrease in daily dosage; (2) small initial doses with daily in-

crement until the desired effect was obtained or toxic symptoms developed.

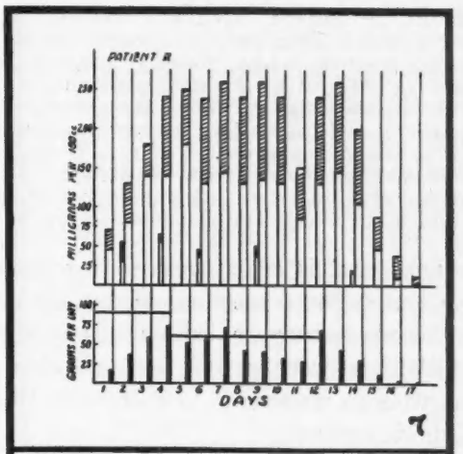
In the treatment of other infections rather massive dosage (over 100 grains per day) has often been employed. Several patients undergoing such treatment have been followed biochemically. In this connection it is interesting to note that body fluids, other than blood and urine, have been examined and found to contain considerable quantities of sulphanilamide. When the tissues are "saturated" with the drug at any particular dosage the concentration in the tissue fluids is close to, but usually slightly lower than, that in the blood. For example, patient N., with streptococcal meningitis, was given 125 grains of sulphanilamide per day. At the end of the first day the blood contained 6.1 mg. per cent and the cerebrospinal fluid contained 4.8 mg. per cent. By the end of the fourth day the blood contained 11.7 mg. per cent. The patient died on the fifth day, at which time the blood contained 9.7 mg. per cent and a mixture of cerebrospinal fluid and pus (obtained at autopsy) contained 10.3 mg. per cent. These biochemical findings are similar to those already reported by other workers.

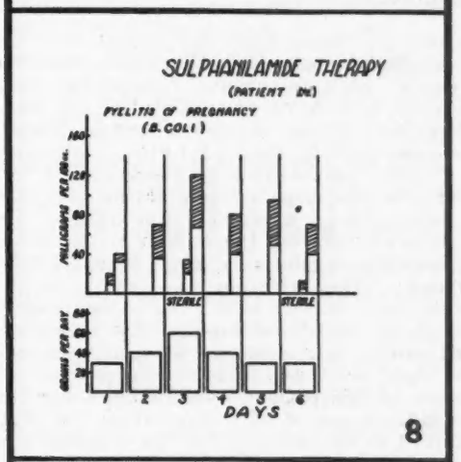
Two fluids not previously reported upon, saliva and sweat, have been examined. Both contained sulphanilamide.

Large initial dosage.—It has been a general practice among urologists to treat specific urethritis with rather large initial doses of sulphanilamide, usually 80 grains per day. This procedure has also been used in the treatment of pyelitis and cystitis, since it was believed that the rapid attainment of high concentrations in body fluids would result in speedy cure. Data from typical cases are presented below.

Patient T., female, aged 24; weight 110 lbs.; bilateral pyelitis and cystitis. Non-protein nitrogen 34 mg. per cent on March 31st, 40 mg. per cent on April 11th. Hæmoglobin 70 per cent, white cell count, 9,800 Following eight days of sulphanilamide therapy (total drug ingested, 340 grains), hæmoglobin was 65 per cent, white cell count, 9,800. In this case, as in all others, fluid intake was controlled to produce approximately 1,500 c.c. urine per day. Only one blood specimen was taken each day; this was collected just before giving the initial dose of the next 24 hour period. The total 24 hour urine was collected for analysis. There was some difficulty in obtaining complete 24 hour urines from patients with frequency, but in the cases reported we believe the losses were small. The data obtained are shown graphically in Fig. 5.

The significant features in this case are: (1) slightly elevated blood concentration on the second day and slightly low urine concentrations, considering the dosage (evidence of accumulation of drug in body); (2) the sudden disappearance of pus from urine during the course of the second and third days; (3) coincident with the clinical improvement there was a sudden increase in the excretory ability of the kidney, as evidenced by the very high concentrations of sulphanilamide in the urine, in spite of the decreased dosage (40 grains) on the third day.





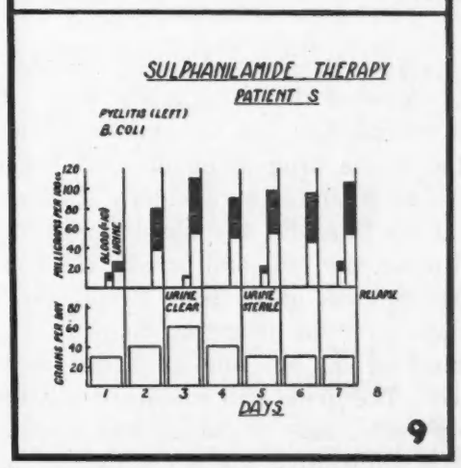


Fig. 7.—Patient with renal calculi and infection. Symbolism same as in Fig. 6. In the lower part of the figure the heavy horizontal line represents total dose per day, the black columns represent the amount of drug recovered in the urine. Some urine was unavoidably lost on days 9, 10 and 11. Larger fluid intake than usual on the 11th day is reflected in the lowered concentration of drug in the 24 hour urine. Note that during first four days output less than intake (drug accumulating in tissues); for five days after discontinuing the drug it continues to be eliminated in the urine. **Fig. 8.**—Biochemical response of patient to step dosage. Note much lower blood and urine concentrations than in previous cases, yet infection was controlled quickly. **Fig. 9.**—Biochemical response to step dosage. Note very low blood concentrations—more efficient elimination than in patient D.V.—and rapid clearing of urine. Note also the relapse due to premature withdrawal of the drug.

Patient D., female, aged 27; weight 135 lbs., bilateral pyelitis. Non-protein nitrogen 29 mg. per cent, before treatment; hæmoglobin 70 per cent. After two days on 80 grains of sulphanilamide the blood concentration was slightly higher than expected (7.5 mg. per cent), and the patient became nauseated, but no other toxic signs appeared. Owing to severe nausea on the fourth day the drug was omitted on the fifth day. Total drug ingested in eight days, 340 grains. For details as to dosage and response see Fig. 6.

The next case is cited because this patient's kidneys had suffered mechanical damage. It is also of interest because rather large doses of sulphanilamide were given for several weeks, and an attempt was made to determine the sulphanilamide balance.

Patient R., male, aged 39; weight 147 lbs.; bilateral nephrolithotomy in 1934; now had bilateral renal calculi with infection. Non-protein nitrogen, February 23rd to April 21st, 45 to 54 mg. per cent. Phthalein test, 72 per cent in 2 hours. Water test, fair (specific gravity 1.005 to 1.015). CO_2-combining power (during sulphanilamide therapy), 54 volumes per cent. In the hope of eliminating the infection which was producing a very alkaline urine, and which we felt was accelerating the growth of the stones, the patient was given relatively large doses of the drug, for 12 days. The infection was improved, and the urine eventually became acid. Toxic symptoms ensued and the drug was discontinued. The infection soon returned and the urine became alkaline once more.

The blood levels and urine concentrations (24 hour specimens) of this patient were followed for 17 days. This includes a period of 5 days after the drug was discontinued so that the elimination of sulphanilamide from the tissues might be studied (Fig. 7).

In spite of the known kidney damage this patient excreted the drug fairly well. There was an initial delay in the excretion, but this was due to the drug going into the tissues to saturate them and not to kidney dysfunction, since at no time did the blood concentrations exceed 6 mg. per cent and usually the free sulphanilamide was only about 3 mg. per cent. Five days after the drug was stopped the blood was analyzed but no sulphanilamide could be detected. The urine still contained a little (12 mg. per cent), most of which was conjugated. The total sulphanilamide accounted for in the urine was only 80 per cent of the ingested drug. The deficit was probably mainly due to the difficulty in collecting complete urines over such a long period, especially from patients with frequency.

The large initial dosage regimen rapidly produces high concentrations of sulphanilamide in the tissues. However, it has been our experience that although effective in sterilizing the urine these doses often cause considerable upset such as nausea, headache, fever, etc., to the patient. It is our impression that most patients with pyelitis and cystitis do not tolerate well large initial doses (80 grains) of sulphanilamide. Fortunately, simultaneous bacteriological studies done by Dr. P. H. Greey, led us to believe that much smaller doses might be equally effective in eradicating the infection without producing marked toxic reactions. This led us to adopt the step-dosage procedure described in the following section.

The step-dosage procedure.—Two examples to illustrate the biochemical response of patients on increasing dosage will be given.

Patient D.V., female, aged 22, weight 135 pounds; pyelitis of pregnancy. Non-protein nitrogen 38 mg. per cent; hæmoglobin (before treatment) 68 per cent. CO_2-combining power (before) 50 volumes per cent; third day of treatment, 40; fifth day, 41 volumes per cent.

The dosage and resulting blood and urine concentrations are shown in Fig. 8. The significant point to note is that the blood concentrations (and therefore those of the tissue fluids) are very much lower than on the large initial dosage regimen. The patient was not upset by the drug, yet the infection was quickly eradicated. Note the fall in the CO_2-combining power of the blood.

Patient S., female, aged 33, weight 155 lbs.; ruptured kidney with infection. Hæmoglobin 65 per cent; red cell count, 5 million; white cell count varied from 15,000 to 27,000 between March 27th and May 6th. Non-protein nitrogen, April 6th, 42 mg. per cent. Sulphanilamide was started on April 6th. CO_2-combining power, April 7th, 50 volumes per cent; April 9th, 50; April 11th, 41; April 13th, 43.

The significant biochemical features (see Fig. 9) are the low blood and urine concentrations (very similar to those in the previous case) which sufficed to sterilize the urine, at least temporarily. This patient also showed a lowered CO_2-combining power. The relapse noted upon withdrawal of the drug was detected bacteriologically at once, but was not apparent, clinically, for several days. The significance of this will be discussed in a subsequent communication, where a modification of the step-dosage procedure which prevents these relapses will be described.

Abnormal responses to very large, or very small dosage.—In this section atypical biochemical responses of patients will be described. In cases with septicæmia, meningitis or other serious infections it is generally considered advisable to give sulphanilamide in sufficient dosage to raise the blood concentration above 10 mg. per cent. However, several patients have been seen whose kidneys could eliminate such remarkable quantities of sulphanilamide, over a period of many days, without any appreciable accumulation of the drug in the tissues that it was very difficult to reach the reputedly effective therapeutic concentrations. One such case will be described.

Patient Sul., male, aged 40; multiple abscesses (liver, lungs, and kidneys). Hepatic abscess, drained on admission to hospital, contained anaerobic streptococci and *B. coli*. In spite of relatively large doses (90 to 160 grains per day) during the first two weeks of this treatment the blood concentrations were rather low (3 to 8 mg. per 100 c.c.) and it was suspected that the drug was not being absorbed. Chemical examination of the fæces, however, revealed only neglible quantities of the drug. After four days on sulphanilamide therapy the patient's temperature fell from 106° to normal and he appeared to be recovering. The drug was discontinued. One week later there was recurrence of the fever with signs of acute inflammation in the lungs. The patient rapidly became extremely ill. The original dosage of sulphanilamide was resumed at once, without improvement in the condition. The dose was increased without beneficial effect. In the later stages of the treatment, on a dosage of 200 grains per day, the concentration of sulphanilamide in the blood reached 15 mg. per cent free and 20 mg. per cent total. These higher blood levels were obtained after a severe reaction to a blood transfusion in which the kidneys were involved (hæmaturia, albuminuria and slight retention of fluids). At autopsy, although the liver abscess was healed, the lung abscesses had persisted, and multiple minute abscesses of both kidneys were discovered. These abscesses, plus the damage to the kidneys, probably accounted for the rather sudden increase in the concentration of sulphanilamide in the blood of this patient, who had previously excreted the drug with remarkable efficiency.

In contrast with the biochemical response of the above patient, may be cited that of

Patient P., female, aged 55; chronic nephritis and cystitis. This patient was given 10 grains t.i.d. for two days, by which time she had severe malaise. On the morning of the third day the blood concentration was found to be 13.0 mg. per cent of free sulphanilamide with a total of 21.1 mg. per cent. The drug was immediately discontinued.

A similar case showing even more marked retention of sulphanilamide was that of

Patient So., male, aged 71; chronic bilateral pyelonephritis. This patient's non-protein nitrogen had gradually risen during a period of two years from 46 to 90 mg. per cent. During this period he suffered from intermittent pyrexia, which was attributed to exacerbations of the pyelonephritis. When given sulphanilamide during one of these attacks, blood concentrations of 8 mg. per cent resulted from the very small dose of 10 grains daily. Further evidence that sulphanilamide was being retained in the body due to kidney dysfunction and not entirely to absorption of the drug by the tissues was the very low concentration of the drug (10 to 20 mg. per cent) in the urine.

DISCUSSION

Since a careful study of the cases described will give a good general impression of the blood and urine concentrations to be expected from any of the usual dosage procedures no lengthy discussion of the results is considered necessary. Limitations of space prevent further detailed description of our experiments, but the more outstanding points (most of which are illustrated in the data above) are summarized below.

1. The larger the individual dose, the higher is the peak of the blood concentration curve, and the earlier this peak occurs.

2. Maximum blood concentrations following *single* doses are not proportional to the dose, but increase only slightly on doubling or trebling the dose, provided kidney function is normal.

3. The peak in the blood concentration is reached usually about 4 to 6 hours after a single 15 grain dose, and about 2 to 5 hours after a single 30 grain dose. In children the peak is earlier (1 to 2 hours after 10 grains).

4. Either taking the drug in solution or drinking reasonable quantities of water after swallowing the pills favours absorption, and thus results in a slightly earlier and higher peak in the blood (compare Figs. 1 and 2).

5. With normal kidney function even repeated large doses (20 to 30 grains every few hours) will not raise the blood concentration above about 5 to 6 mg. per cent until the tissue fluids are saturated. This usually takes several days. However, with slightly impaired kidney function the blood concentrations rise more rapidly, and in some cases (with more marked dysfunction) even small doses (15 to 30 grains per day) may result in very high blood levels (12 to 25 mg. per cent) within three or four days. It is for this reason that biochemical control of patients on sulphanilamide therapy is advocated.

6. Patients on larger dosage regimens (over 40 grains per day) often show a fall in CO_2-combining power. This may be counteracted by giving sodium bicarbonate.

7. On constant fluid intake the concentration of sulphanilamide in the urine is almost directly proportional to the dose ingested.

8. Increasing the fluid intake does not cause an increased rate of excretion of the drug in subjects with *normal* kidney function. In the treatment of infections of the kidney or bladder high urinary concentrations are desired, and fluid intake should therefore be controlled (the 24 hour urine should not exceed 1,500 c.c., and it is better to try to keep under 1,200 c.c. if the patient does not complain).

9. Following a single dose about 45 to 60 per cent is excreted in the urine during the first 24 hours. At first the sulphanilamide in the urine is nearly all free, but toward the end of the 24 hour period about 75 per cent of the drug excreted is in the conjugated form. The average fraction conjugated for the first 24 hour period is usually 40 to 60 per cent of the drug eliminated.

10. After several days on repeated constant dosage the quantity excreted becomes about

equal to the quantity ingested (as long as kidney function is normal), and about 40 to 65 per cent of this is in the conjugated (inactive) form. In other words, about one-half of the drug given is rendered therapeutically inactive before it reaches the urine.

11. No simple relationship has yet been found between any one of the usual kidney function tests and the ability to eliminate sulphanilamide. While certain patients with a somewhat elevated non-protein nitrogen can excrete the drug with fair efficiency, others (with even lower non-protein nitrogen) may not. In a very rough way the phthalein test may suggest the probable response of the kidneys to sulphanilamide, although the correspondence is not always good. The only accurate indicator of sulphanilamide excretion appears to be sulphanilamide itself.

12. It is not safe to predict what blood or urine concentrations will result from any particular dosage regimen, since patients vary considerably in their handling of sulphanilamide. Blood concentrations (at constant dosage) depend upon the relative rates of the processes of absorption, conjugation and excretion, any one of which, or all, may vary from patient to patient or in the same patient from time to time as his condition changes.

13. Since patients on constant dosage eventually (within 2 to 4 days) reach an equilibrium between intake and output it is generally possible by adjusting the dosage to maintain blood concentrations at any desired level. The size of the individual doses and the frequency of giving them varies considerably; these can only be determined by trial and error for each patient. In general, the dose should be given every four hours to maintain high tissue concentrations such as are necessary for control of fulminating infections. The size of the individual dose necessary to maintain blood concentrations above 10 mg. per cent on such a routine usually varies from 20 to 30 grains (*i.e.*, 120 to 180 grains per day), but less may suffice in some cases. Since sulphanilamide is not without toxic effects high dosage should not be continued longer than is necessary to effect clinical improvement. Too rapid withdrawal of the drug may permit a relapse; the dose should be cut down gradually.

14. In the treatment of infections of the urinary tract, experience indicates that high concentrations of the drug in the urine are more important than are high blood concentrations. Smaller individual doses (5 to 20 grains) than are used for other infections (given three or at most four times per day) with fluid restriction usually produce adequate therapeutic concentrations in the urine.

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PELVIC ENDOMETRIOSIS*

(REPORT OF 40 CASES)

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THIS paper is confined largely to a clinical discussion of pelvic endometriosis, with analysis of 40 cases operated on in the gynæcological ward of the Toronto General Hospital.

Pelvic endometriosis is characterized by the occurrence of multiple islands of endometrial glands and stroma scattered throughout the pelvic peritoneal cavity, blood-filled cysts of the ovaries, and extensive pelvic adhesions. This ectopic endometrium undergoes the same cyclic histological change as the endometrium of the uterus, showing premenstrual congestion, menstrual bleeding, and, with pregnancy, decidual reaction.

This ectopic endometrium is most commonly found on the ovary, but may in the more extensive cases involve any structure in the pelvis, including small and large intestine, appendix, bladder and omentum. It is occasionally found in the inguinal canal, in abdominal scars following pelvic operations and Cæsarean section, and occasionally in the umbilicus. Endometrial adenomas have been demonstrated in pelvic lymph glands and in the lower vagina. These more unusual situations of ectopic endometrium are interesting chiefly when considered in relationship to the etiology of endometriosis and will not be discussed in this paper.

At this point it might be well to correlate adenomyoma of the uterus and endometriosis.

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The two conditions are both characterized by the presence of endometrial glands and stroma in abnormal situations. In the former, the ectopic tissue is found in the wall of the uterus and is associated with hypertrophy of the uterine muscle, while in the latter the endometrial adenoma is situated outside the uterus or invades the uterus from its serosal aspect. Dougal[1] suggests that both lesions be considered as endometriosis and designates them as internal and external. These two lesions, having the one common factor, the presence of endometrium in abnormal situations, are not otherwise related. The etiology of adenomyoma of the uterus was established by Cullen[2] as a direct invasion of the uterine wall by the basal layer of the endometrium, while the origin of distant endometrial adenoma is still a controversial subject. There is only a casual association of the two diseases. In a series of 124 surgical specimens of adenomyoma of the uterus, diagnosed in our laboratory, so-called external endometriosis was only associated in 4 cases.

During the past 10 years there has been a marked revival of interest and study of these more distant adenoma of the endometrial type. In 1921 Sampson published his first article on endometrial adenoma of the ovary entitled "Perforating hæmorrhagic cysts of the ovary"[3] and in 1922 published a second article "Life history of ovarian hæmatomas".[4] He particularly emphasized two features of endometriosis, firstly, its widespread distribution throughout the pelvis and, secondly, its frequency. He found evidence of endometriosis 98 times in 332 gynæcological operations. The widespread distribution of the endometrial adenoma suggested to Sampson the theory that this endometrium-like tissue was implanted upon the pelvic peritoneum. He proposed that this apparent seeding of endometrium was due to the escape through the Fallopian tube of menstrual blood containing fragments of desquamated endometrium. He demonstrated that the ovary is the most frequent site of ectopic endometrium, and, due to its situation, the most likely structure upon which regurgitated endometrium would fall. The ovary then might act as an intermediary host, and with cystic development and menstruation of this endometrium further dissemination and implantation would occur.

The common embryological origin from cœlomic epithelium of pelvic peritoneum, germinal epithelium of ovary, tubal mucosa and endometrium, closely links these epithelial elements. Iwanoff[5] suggested the serosal origin of pelvic adenoma of the endometrial type and was supported by Robert Meyer.[6] Novak adheres to this view and has been the chief opponent of Sampson's theory. That such a heteroplasia of serosa and germinal epithelium occurs has been demonstrated, and older writers felt that inflammation was the exciting cause. More recently excess stimulation by œstrin has been offered as the initial cause.[7]

A discussion of the theories of the origin of endometriosis does not fall within the sphere of this paper. The subject is a controversial one, and the gynæcological literature over the past ten years contains innumerable articles discussing this phase of the disease. The truth probably lies in a combination of the serosal theory of Iwanoff and a modification of Sampson's theory of implantation.

Endometrial adenomas are most frequently found in the ovary. With invasion of the ovarian stroma by endometrium or relining of follicular cysts by endometrium cystic spaces lined by endometrial glands and stroma are formed. These cysts, filled with old menstrual blood, form the so-called "chocolate cysts" of Sampson. The cysts are usually small, but may before perforation or rupture occurs reach a considerable size. Small superficial areas of endometriosis on the ovary appear as retracted puckered areas with a centrally situated dark bleb which, when punctured, exudes a small amount of tarry blood. Similar areas of endometriosis are frequently found scattered in a discrete manner on the posterior aspect of the uterus, peritoneum of the cul-de-sac and rectum. With menstruation of the ectopic endometrium small areas of peritonitis occur, which, with organization of the blood and resulting exudate, lead to the formation of dense fibrous adhesions, in the more extensive cases firmly binding together uterus, tubes, ovaries and bowel. The continued invasive qualities of the endometrium may lead to extension through the vaginal vault or into recto-vaginal septum.

Involvement of bowel wall with mass-formation sufficient to produce symptoms of obstruction may occur. Sampson[8] discussed this important aspect of endometriosis and pointed out

the danger of mistaking endometriosis of rectum or sigmoid for carcinoma. He reported one case in which such a mistake was made and we have seen three similar ones. In one an abdominal-perineal resection of the rectum was performed with permanent colostomy. Such an error in diagnosis is obviously a grave one, particularly when an extensive radical operation is employed in treatment. Minor degrees of rectal and sigmoid involvement occur in approximately half the cases of endometriosis. In our series of 40 cases 23 showed rectum or sigmoid either directly invaded by endometriosis or involved in extensive adhesions. In most cases of rectal or sigmoid invasion there is extensive pelvic endometriosis, but this is not always so and occasionally a careful examination of ovaries and pelvic peritoneum may be required before characteristic areas of endometriosis are discovered.

The signs and symptoms of pelvic endometriosis depend on the extent of the disease, the structures involved, and the presence of fibroid tumours of the uterus. Fibroids are very commonly associated with it. In this series of 40 cases these new growths were present in 15. The symptoms occurring in this group of patients correspond with those reported by other writers, and were, in order of frequency, abdominal pain, menorrhagia and dysmenorrhœa. The rupture of an endometrial cyst will occasionally produce acute localized peritonitis which may be mistaken for acute appendicitis. No patient in this group was operated on as an abdominal emergency since in public ward practice these patients are not as a rule admitted to the gynæcological service.

Abdominal pain was the commonest symptom, occurring in 30 of the 40 patients in this series. The character of the pain varied and was apparently difficult for the patient to describe. Dragging lower abdominal pain, situated just above the inguinal ligament, with periods of exacerbations and a tendency to radiate downwards, was most constantly described. The pain is frequently exaggerated in the immediate premenstrual and menstrual phase, this exaggeration being noted in 10 cases.

Disturbance of the menstrual flow was the second most common symptom, occurring in 22 cases, menorrhagia in 11, metrorrhagia in 4, and a combination of both in 7. It is difficult to evaluate the rôle played by endometriosis in the production of disturbances of menstrual flow due to the frequent association of myomata. Of the 22 cases with a disturbance of menstrual flow, 12 had fibroids in the uterus. Whatever the cause, in this series of 40 cases 28 patients presented a changed menstrual function, the change involving either flow, cycle, or pain.

Dysmenorrhœa, usually of gradually increasing severity, was the chief complaint in 9 cases, although menstrual pain was complained of by 19 patients. In the majority of cases the pain was dull and constant in character, with periods of crampy exacerbations sufficient to temporarily incapacitate the patient.

Endometriosis occurs most commonly in patients between 30 and 40 years of age. In this series the average age was 36.6 years; the youngest patient was 21 and the oldest 49. There were 6 patients in the twenties, 24 in the thirties and 11 in the forties.

Sterility and low fertility are commonly associated with endometriosis. In this series, the average number of pregnancies in the married patients was two. There were 8 married patients without children. Only one patient's main complaint was sterility. These figures are difficult to evaluate, but it does seem reasonable to say that for a group of public ward patients the average of 2 pregnancies is low. The average number of years since the last pregnancy had occurred in the parous group of patients was 9.6. Dougal,[1] in a much larger series of cases, found in 32 per cent that the interval between the last pregnancy and the time of operation for endometriosis was 10 years. These figures emphasize the association of endometriosis and relative sterility. There were 6 abortions or miscarriages in this group. Dyspareunia was not a common complaint. Pain on defæcation was complained of in only one case, which is surprising when the frequency of involvement of rectum and sigmoid is considered.

Of the 40 cases in this series 1 in 4 had had some previous gynæcological operation, 7 laparotomies, and 3 dilatations and curettages, an unusually high figure which may be of some significance in etiology.

The findings on bimanual examination obviously depend on the extent of the disease. With involvement of only one ovary a fixed tender ovary with tenderness exaggerated in the premenstrual phase is usually evident. With involvement of the pouch of Douglas and adhesions between cervix and rectum, which occurs very early in the disease, a characteristic but indefinite puckered thickening is evident in

the posterior fornix. With more extensive involvement of the pouch of Douglas and recto-vaginal septum, definite tender mass-formation is evident with limitation of movement of the cervix. When deep invasion of the cellular tissue at the vaginal vault has occurred inspection of the posterior fornix may show invasion of the vagina by small endometriomata, identified as purplish blebs in the mucosa which when punctured exude the characteristic tarry blood of the endometrial cyst. This was observed in 2 cases in this series.

With formation of multiple chocolate cysts, matting together of tubes, ovaries, and bowel, large indurated tender masses are formed, suggesting pelvic inflammatory disease. The very frequent association of myomata causes an irregular, enlarged hard uterus. It has been suggested that retroversion of the uterus is common in pelvic endometriosis and is of some etiological significance if Sampson's theory of retrograde flow of menstrual blood through the tube is believed. In this series of cases 9 uteri were retroverted.

The treatment of pelvic endometriosis is surgical, and whether a radical or conservative operation is performed depends on the age of the patient, the extent of the disease, and the structures involved. In this series one or both ovaries were the site of endometriosis in 37 cases. Moderate to extensive pelvic adhesions were present in 28 cases, and in 23 cases the rectum and sigmoid were either directly invaded by endometriosis or were extensively involved in adhesions. It is not surprising then that bilateral salpingo-oöphorectomy and hysterectomy were employed in 32 cases. Eight cases were treated conservatively by resection of the ovaries and separation of adhesions. Technical difficulties of operation are great, due to the density of the adhesions. Sharp dissection is usually required throughout as lines of cleavage are practically non-existent. Extensive dissection in the recto-vaginal septum to remove endometriosis or resection of bowel is however rarely required, as with bilateral oöphorectomy further hormone stimulation to the ectopic endometrium ceases, further invasion is arrested, and the endometrial adenomas become atrophied.

The chief risk of operation is injury to the rectum or sigmoid, which may escape recognition. One patient in this series died from post-operative peritonitis. The cause of peritonitis however was not determined as no post-mortem examination was permitted.

SUMMARY

Forty cases of pelvic endometriosis operated on in the public gynæcological service of the Toronto General Hospital have been reviewed.

The age-incidence of the disease, the incidence of relative sterility, and associated fibroid tumours of the uterus correspond with other reported cases.

The chief symptoms in order of frequency were abdominal pain, menorrhagia and dysmenorrhœa. The rectum and sigmoid were involved either by adhesions or direct invasion of the endometrial adenoma in 23 cases.

The danger of mistaking such endometrial invasion of bowel for carcinoma has been mentioned, and the tragedy of employing radical operation, due to such a mistaken diagnosis, has been emphasized.

The treatment of pelvic endometriosis is surgical and depends largely on the extent of the disease. Unfortunately, in the majority of the cases bilateral salpingo-oöphorectomy and hysterectomy are required for a permanent cure.

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THE DIAGNOSIS AND TREATMENT OF THE COMMON DISORDERS OF MENSTRUATION*

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PRACTITIONERS everywhere are besieged by the vendors of the different hormonal preparations which are recommended for the abnormalities of menstruation. We should have some rational method of diagnosing part or all of the hormonal situation in these clinical conditions, since diagnosis must precede any proper therapy, whether it be endocrine, surgical, or a combination of the two.

The following is an attempt to present such a method of diagnosis, based upon estimations of œstrogenic substance in the blood carried out on the author's private patients. Admittedly determinations of female sex hormone in the blood do not give a complete picture of what is happening in the complex endocrine system of the body. However, the œstrogens seem to be the effector agents in so many of the uterine phenomena to be discussed that for practical purposes they may be considered by themselves and very satisfactory diagnostic and therapeutic measures be based upon their assay alone. Moreover, it is advantageous, where possible, to use one simple and rapid test for these cases rather than to attempt in each instance to correlate assays of urinary pregnanediol,[1] blood and urinary œstrogens,[2] and urinary prolans A and B.[3] This is especially true because the methods for urinary œstrogens and prolans leave a good deal to be desired in the way of accuracy and simplicity, and the test for pregnanediol in urine is exacting. Moreover, we do not know the precise quantitative relationship existing between the amounts of prolans and œstrins excreted from the body and the quantities of such substances simultaneously active in the circulation.[4]

There are several methods for the assay of œstrogens in the blood. Frank,[5] Siebke,[6] and Fluhmann[7] have published biological assay methods. However, Schlossberg and Durruty[8] have severely criticized the one most widely used, *viz.*, Frank's quantitative technique. The author has published[9, 10] and extensively used a simple biochemical test which is qualitative, only very roughly quantitative, but which can be carried out in less than two hours' time, and requires only 6 c.c. of fresh uncitrated blood, which is taken as for an ordinary Wassermann test. His experiences with this test as a criterion for the diagnosis and therapy of the common menstrual abnormalities are outlined below.

MENORRHAGIA

Menorrhagia appears to be related to an excessive accumulation of œstrogen in the blood[11] in many instances in which no mechanical causative factor can be ascertained. As Frank has demonstrated that the blood œstrogen is highest in the three days before and on the first day of the period, and that it is low just after the termination of the flow, his work has yielded an approach to this problem (Fig. 1).

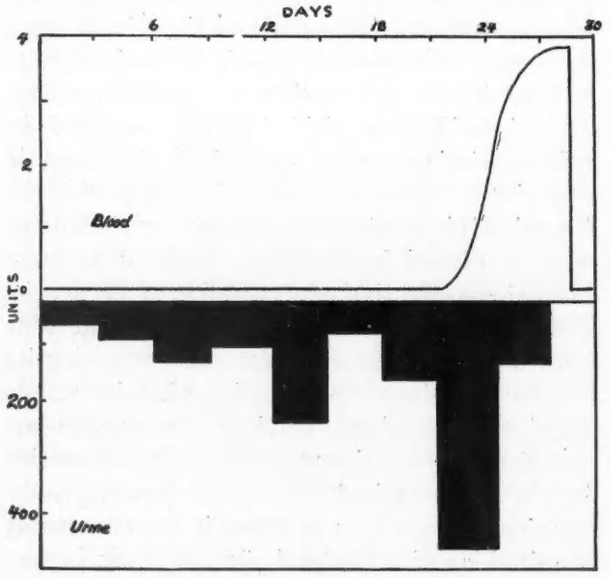

Fig. 1.—Occurrence of œstrogenic substance in the blood and urine of normal women during the menstrual month (from R. T. Frank).

The author's test is so adjusted that it gives a positive result just before and a negative just after a normal menstruation. Accordingly, if one tests the patient's blood just at or after the end of the menses and finds an excess of œstro-

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gen still, in spite of the increased loss of œstrogen in the menstrual blood and urine during menstruation and afterward, he is justified in concluding that there was an excess of œstrogen before the period, and hence that one or other of the anti-œstrogens might rationally be used in treatment.

If there is not a rapid response to such therapy, curettage should be done, preferably in the premenstrual phase, to determine whether or not something of a gross character has been overlooked. The conclusion that the menorrhagia is endocrine may have been reached too readily, but it is a justifiable preliminary assumption in patients under 35 years of age, and we rarely subject a patient below that age to a curettage, which is, after all, a moderately expensive and often useless procedure. It may be objected that a study of the endometrium is demanded for endocrine diagnosis, but any one familiar with the recent literature knows how fallacious can be the deductions drawn from curettings.[12] At or near the menopause fibroids are frequently accessory or principal etiological factors in the production of menorrhagia, and, of course, malignancy must always be kept in mind. But fibroids may be a harmless feature of the picture, and endocrine therapy be the thing needful to correct the patient's complaint, rather than any surgical procedure. This point is too frequently overlooked.

OLIGOMENORRHŒA

Oligomenorrhœa, or scanty menstruation, on the other hand, is frequently associated with a deficiency of blood œstrogenic substance just before menstruation begins, and this will be revealed by testing the blood as indicated. One should not assume such an œstrin deficiency in every case, however, for occasionally, as in the rare amenorrhœa, there is actually in these women an excess of œstrogens in the bloodstream before the flow. Where the oligomenorrhœa is related to œstrogen deficiency, the ordinary dosages, at least, of œstrogens will not increase the amount of flow, but often will correct any associated dysmenorrhœa. But if the scanty flow occurs with a high blood œstrin, the treatment indicated is just the reverse of that usually given, for an anti-œstrogen, such as thyroid extract, will actually increase the amount of flow.

IRREGULAR MENSTRUAL CYCLES

Irregular menstrual cycles appear to be due, largely at least, to variations in function of the corpora lutea.[1] Whether such changes, in turn, are primarily due to variation in function of the anterior lobe of the pituitary remains to be seen. However, correction of the individual periods will usually cause the altered cycle to adjust itself. Thus one may assume for practical purposes that an average quantity of blood loss every two weeks corresponds to a menorrhagia every four weeks, or that an average flow every six to seven weeks corresponds to what would have been an oligomenorrhœa had it occurred every four weeks. Acting on such assumptions, one can sometimes correct altered cycles rather easily.

DYSMENORRHŒA

Dysmenorrhœa is a very complex topic in itself. When due to endocrine dysfunction it can usually be studied by œstrogen analyses made just before and just after the menstrual flow, and suitable treatment may be undertaken accordingly. When endocrine therapy seems ineffective one should curette for submucous fibroids, and, if none are found, suspect endometriosis.

It would appear that where there is too much œstrogen in circulation before the menses, the uterus exhibits excessively strong contractions. Where there is not enough œstrin the uterus may exhibit none whatever.[13] Just why there should be pain with the latter is not yet clear, but the pain associated with excessive uterine contractions may be equalled by the non-contracting corpus. Moir has advanced the idea that powerful uterine cramps may cause temporary muscle ischæmia,[14] but Lackner and Krohn could not confirm this. The pain mechanism is unexplained, therefore.

Resection of the presacral nerve plexus should be mentioned, of course, in any discussion of dysmenorrhœa. However, if endocrine diagnosis and treatment were properly carried out such a surgical procedure would find only a minimal place in our therapeutics. It is not easy, and entails the danger associated with laparotomies.

It is so common for the low œstrin type of dysmenorrhœa to be associated with menstrual irregularity that it is frequently difficult to know when to administer œstrin to such women. It seems to me that what is really needed for

such cases is an intravenous preparation of œstrin of moderately high unitage. This is something for the pharmaceutical houses to ponder.

AMENORRHŒAS, INCLUDING THE MENOPAUSE

The amenorrhœas, either during sexual maturity or at the climacteric, are also a thorny problem. However, the essential in their study, so far as we at present know, seems to be to determine whether or not the body is still proceeding through the endocrine changes characteristic of its usual menstrual cycles (although in such cases this is not revealed by periodic uterine hæmorrhage). Such endocrine cycles may continue for twenty years or more after menstruation has ceased. Therefore, it can be readily seen how fallacious it is to assume that ovarian activity has ceased merely because periodic bleeding has ceased. Examinations of the blood for its œstrogen content, made every five to seven days, should tell us whether or not there is either a constant absence of appreciable quantities of œstrogens, or a constant low value, or a true cycle of the kind seen in normal, regularly menstruating women.[4] If a cycle is discovered one is given a rational means of timing treatment in order to coincide with or neutralize nature's effort to produce cyclical hæmorrhage, depending upon whether the case is a maturity or a post-menopausal amenorrhœa, respectively.

Perhaps it is radical to view the menopause as just another amenorrhœa, but what is it more than that? It may be secondary or primary, that is, there may still be œstrin cycles for years during which such patients may be made to menstruate normally,[15] or there may be no cycle. Fertility may persist, which is the best evidence of normal ovarian function. Indeed, menopausal bleeding is frequently a high-œstrin phenomenon, when not due to malignant growths or fibroids, and the women who become obese at that time often owe their weight gain to a hypothyroid state, which in turn is very frequently associated with high blood œstrin.[16]

What are we to think of the mental states of menopausal women? These are not all to be ascribed to the menopause *per se*, for we would hesitate to ascribe a puerperal psychosis to pregnancy amenorrhœa. In the forties these women are under unusual strains, quite apart from any alteration of menstruation. Their husbands enter a second childhood and find other women more attractive as their own wives fade. Their children enter the dangerous twenties and cause worry about their careers, their scholastic success at the increasingly difficult college levels, or by their choice of mates. Perhaps the woman's own economic future becomes more obviously precarious. In the thirties there was still hope that she and her husband might recoup their fortunes. In the forties this hope has gone. Old age begins to loom close, especially to lonely "old maids". Back-fence gossip, too, has taught women that the menopause is a terrible crisis which often leads to insanity or invalidism. Several such harrassing factors may be additive. It would seem, therefore, that many so-called menopausal complaints are not to be ascribed to the menopause itself. Hence the success of so many differing types of therapy, notably the indiscriminate use of œstrogens. About one-third of these women already possess a high œstrogen.[17, 18] Yet series of cases are reported from various clinics in which practically every woman has been benefited by œstrin! Pratt has demonstrated the fallacies of this type of therapy best, perhaps. He cured menopausal women with everything, including saline hypodermics.

It seems to me that any treatment of amenorrhœa, menopausal or otherwise, will be carried on blindfolded until such time as the importance of testing for œstrogen cycles in the bloodstream is recognized. In many cases, in which there is no uterine atrophy, there seems little reason to attempt to re-institute the menses, for the body may display a menstrual cycle just lacking uterine bleeding. Indeed, the exhibition of œstrogens will rarely produce continued menstrual-like bleeding, but merely one or two cyclical hæmorrhages before amenorrhœa returns. The only amenorrhœic women to whom one can really promise much are those having hypothyroidism. As I have had no experience with the newest preparations of pregnant mare's serum, I have not ventured to say anything here of their place in the therapy of amenorrhœa.

GENERAL REMARKS

One cannot condemn too heartily the present tendency to haphazard treatment of women suspected of endocrine abnormalities with preparations whose action is unknown, and which are administered without careful preliminary diagnosis. The pharmaceutical houses are partially to blame, for it is not rare to see in

their literature that one of their products is good for "dysmenorrhœa", for example. But we know that dysmenorrhœa is a symptom of uterine or extra-uterine dysfunction which can develop from any one of many different causes. Therefore no one thing can ever be good for "dysmenorrhœa". We know that there are at least three types of menopausal women with respect to their blood œstrin levels. How can any single preparation be good for "the menopause"? Women may have a senile vulvitis due to too low a blood œstrogen level or, again, associated with a high level. How can any one thing be used for all cases of "senile vulvitis"? It is therefore not to be wondered at that physicians become dissatisfied with endocrine therapy and its results. But it would be quite as illogical to be disgruntled with digitalis because it is not helpful in both the irregularity of fibrillation and of extrasystoles, or because it helps the tachycardia of myocardial insufficiency but not that of hyperthyroidism! Let us once and for all face the fact that there can be no proper treatment until a diagnosis has been made in each single instance, and let us bear in mind that dysmenorrhœa, or menorrhagia, or amenorrhœa is only a *symptom, not a syndrome.*

In a general way the treatment indicated for patients revealing a deficiency of blood œstrogenic substance is to supply œstrin, and where there is an excess, some anti-œstrogenic substance. The preparations of œstradiol now on the market appear to be the most suitable form in which to administer an œstrogen. These are usually given intramuscularly, as oral dosage is not very potent. Doses are repeated as often as needed clinically, and individuals differ appreciably in their requirements.

The anti-œstrogens are numerous. The common forms, arranged approximately in ascending order of price and effectiveness, are thyroid extract,[19] prolan preparations, wheat germ oil,[20] and progesterone.[21] I say nothing of testosterone proprionate as I have had no experience with it.

If thyroid extract be used, one should probably become accustomed to some one brand and use it always. Different brands differ widely in potency. Thyroid extract is to be preferred, of course, to thyrovarian preparations, for the ovarian principle in the latter can be overlooked. If it were potent its effect would be the reverse of that of thyroid extract, so perhaps it is just as well things are as they are! The patient should be given an initial trial dose of about one-half grain each day, and this should be raised or lowered as indicated by symptoms. Usually the first hypothyroid symptom to improve is constipation or flatulence; then an increased energy on arising in the morning and a little better tolerance of cold are noted. The dosage may be raised until the patient complains of palpitation, insomnia, or sweats and flushes. If hyperthyroidism is thus induced it soon subsides on cessation of the drug, and one can later revert to a smaller dose that will relieve the original difficulties. One should emphasize the fact that readings of basal metabolic rate are frequently unreliable and even misleading indices of treatment. We have given thyroid extract to women whose initial basal metabolic rate reading was as high as +25, and found patients with a reading of –15 or –20 unable to tolerate any of it. A cautious trial of thyroid treatment is the best guide as to the patient's real hypothyroidism. Remember that the hypothyroid woman may be as nervous, as active, and alert, and even as thin, as many a mild hyperthyroid.

Something I have never seen mentioned in this connection is the seasonal variation in thyroid dosage that should be observed. As the available vitamin E in our diet varies during the year, being high from June to September, low from October to January, and still lower from February to May, so the blood œstrogen varies inversely with it[22] and is high in the winter and spring and low in summer. Therefore those who take thyroid extract, an anti-œstrogen, need most in late winter and least or none in the summer months.

The prolan preparations, whether obtained from early pregnancy urine or from placentæ, should not be used in amounts larger than 200 units per dose, as in these larger doses they may have a paradoxical effect and actually produce a rise of blood œstrogen.[23] Their principal advantage is that they act quickly, as when one sees a case for the first time, for example. Some women cannot tolerate thyroid because of its effect on the heart or nerves. Prolan preparations are a God-send to such people.

Wheat-germ oils used should be extracted by cold pressure rather than by solvents, and

should be kept cold from the date of manufacture. They should be no more than eight to ten weeks old if the best results are to be had. The oil does not have the place in the treatment of menstrual disorders that the two products just mentioned have, but on occasion it acts better than either, notably in the relief of high-œstrin dysmenorrhœa.

Progesterone preparations are the active principle of the corpus luteum and may soon be cheaper if processes for their preparation are improved.

It should be emphasized that our endocrine treatment of these disorders is largely aimed at *substitution* for deficient hormone production or *neutralization* of the effects of over-production. We are quite unable in most cases to modify the underlying endocrine habitus of the patient. Pregnancy may do that, or it may occur due to causes beyond our present ken, but we cannot claim credit for doing it deliberately. Just as insulin is no cure for diabetes, so œstrogens or anti-œstrogens do not cure these various menstrual difficulties. They must be continued, just like insulin or thyroid, for lengthy and unknown periods of time. Occasionally the dosage may require modifications as other factors come into play and modify the individual's hormone picture. Thus we must be cautious in using or abusing that word "cure".

It is my personal opinion that a proper trial of endocrine therapy before surgical measures are attempted for these menstrual disorders would very greatly reduce the number of uterine suspensions performed, and greatly decrease the numbers of hysterectomies and öophorectomies. The author has never yet performed a uterine suspension, and owns to a hearty prejudice against an operation which is based on such a misconception of uterine physiology. Since the idea was first advanced in 1854 that the normal uterine corpus should be anteflexed and anteverted, the further construction has developed that the corpus must always lie so to be normal. From 1902 on a series of operations have been devised to "restore" retroverted uteri to normal position, and before the days of endocrines this procedure was widely used in the hope that it would correct menstrual disorders. I fear no hope has ever been more frequently disappointed. Unfortunately the practice continues, although I believe it can be classed with meddlesome obstetrics as the analogous type of gynæcology. From what we now know, the uterus normally is retroverted at birth, and in adult life it is not its position that matters but its lining, its motility, and the kind of ovaries and pituitary gland with which it is linked. Such an alteration of viewpoint is much to be desired amongst the profession.

Curettage is still used by many physicians, especially for menorrhagia and dysmenorrhœa. In these instances, it is merely a placebo or temporizing measure. If performed just before menstruation is due it may or may not tell the pathologist something of the activity of the corpus luteum present, but that is about all one can expect from it, and one needs to know more than that. It seems to me that its main function is in dysmenorrhœa, where it can be used to detect submucous fibroids after the ordinary endocrine measures have failed to give relief, and in very profuse menorrhagias before treatment has had time to take effect.

SUMMARY

1. It is possible to use estimations of blood œstrogenic substance (female sex hormone) to diagnose menstrual abnormalities and give a rational basis for their therapy, where such therapy should be hormonal in nature.

2. Endocrine menorrhagia is usually associated with an excessive blood œstrogen.

3. Endocrine oligomenorrhœa is usually due to the reverse.

4. Irregular menstrual cycles can often be corrected by correcting the individual periods.

5. Endocrine dysmenorrhœa is one of the most interesting fields for the application of this method of attack.

6. In amenorrhœas, during sexual life or after, it is especially important to detect if œstrin cycles are continuing, and if so, just when they are occurring. Many women continue to have these for years after menstruation has ceased. "Menopausal symptoms" are frequently quite unrelated to the climacteric.

7. Generally speaking, menstrual abnormalities related to œstrin deficiency need œstrogens, and those with an œstrin excess need such anti-œstrogens as thyroid extract, prolan, progesterone, or wheat germ oil.

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ETIOLOGICAL FACTORS AND TREATMENT OF CARCINOMA OF CERVIX*

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I WISH to discuss a disease which has been over-discussed in the past, yet remains unsolved, namely, cancer—a disease whose mortality stands second to that of the heart; a disease which has claimed 120,000 persons in the United States during 1932, and accounts for 10 per cent of all deaths in that country. In Canada, a country with a female population in 1931 of 3,371,417 between the ages of 19 and 85, 755 died of carcinoma of the uterus. This figure rose to 964 in 1936. In 1932, 20 per cent of all deaths from cancer of the female genital tract were due to cancer of the cervix. This figure compares favourably with that obtained in our own clinic at the Royal Victoria Women's Pavilion where an organized cancer clinic has been conducted for the past twenty years. You will therefore realize the importance, the magnitude, and the generality of the subject to be discussed.

A limited number of gynæcologists are actually concerned with the technique or application of radium, but we are all responsible for the knowledge of the etiological factors which may give rise to carcinoma of the cervix, and for the ability to make an early diagnosis. I shall speak under the following headings: (1) etiological factors and diagnosis of cancer of the cervix; (2) methods of treatment and results.

Since no definite local etiological factor has been proved to be responsible for cancer of the cervix I must discuss general etiological factors, and will present to you the investigations as they are being carried on in my own centre of learning, in the experimental research laboratories of McGill University and the hospital which I represent.

I shall take you first to Professor Huskins'[1] genetic department and study chromosomal malformations. Professor Huskins published in 1936 an article dealing with spermatocytic chiasma frequency in strains of mice differing in susceptibility or resistance to the spontaneous occurrence of malignant tumours, and found a correlation between low-chiasma frequency and high incidence to mammary-gland carcinoma. The normal resistant spermatocytes showed

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about thirty-three such chiasma frequencies, while the susceptible strains only showed about twenty-seven. C. C. Little[2] found that cancer susceptibility is inherited from the mother and not from the father. Bitner[3] found that susceptibility is acquired through the mother's milk, because if the young resistant strains of mice were nursed by the mother of a susceptible strain these mice became more susceptible to breast cancer. Later experimentation showed that although chiasma frequency in hybrids is not associated with susceptibility it is influenced by the mother's milk. The correlation is still not quite definite. Metz,[4] of Baltimore, has recently shown that there is a wide discrepancy in size relationship of normal chromosomes both in chromatic and achromatic materials.

THE VIRUS THEORY

I shall now take you to Dr. Gruner's research laboratories at McGill University and show you what is meant by "inclusion bodies", and monocytic, or blood cell, reaction to malignant growths. Gruner,[5] published an article on "Intra-cellular structures in monocytes in cases of malignant disease", and showed inclusion bodies of the filamentous, spirillar, and geniculate forms seen in the monocytes in a high percentage of cases of malignant growths and in a very few cases which were clinically non-malignant. He demonstrated monocytic reactions in untreated and treated cases of cervix cancer, and definitely showed what I consider to be of special prognostic value as illustrated in the following table.

RESULTS OF TREATMENT: PROGNOSIS

	Malignancy	*Good*	*Bad*
Leucocytosis	May be increased	Absent	Present
Small lymphocytes	Always low	Rising up to normal	Number remains low
Monocytes	Always increased	Fall to normal	Remains high
Inclusion bodies....	Present	Not seen	.....

Gruner finds a virus present in practically all cases of new growth. He is culturing this filterable, motile organism from breast cancers and injecting rats and monkeys in an effort to produce malignant growths in the breast. He is not sure whether this virus is the cause of cancer or whether it is an early inhabitant of saprophytic growth. Lewis,[6] of Baltimore, has studied blood changes associated with growing tumours in mice and found that there is in the presence of growing malignant tissue a stimulation of the myeloid structures, increasing the number of neutrophile white cells in the peripheral blood and in the blood-forming organs of the host. The increase varies according to the type of tumour. This blood reaction becomes more prominent with the growth of the tumour, but also subsides in those animals where the tumour regresses.

THE HORMONE THEORY

Work has been going on for several years in the department of biochemistry at McGill, investigating relationships of œstrin and other hormones to malignant new growths. It is, however, too early to come to conclusions. Reliable experimenters have already furnished us with interesting data. A. Lacassagne,[7] from the Institute of Radium, Paris, published his results from the œstrogenic hormone treatment of a strain of mice of which some 72 per cent of the females habitually succumbed to adenocarcinoma of the breast. These mice showed an abundant network of ducts in the axillary and inguinal region. In two or three months the glands became cystic and produced tumour-growths of highly mitotic epithelial cells. These animals died in 1½ to 3 months after the appearance of cancer. In the strain of mice in which only 2 per cent of the females developed spontaneous adenocarcinoma weekly injections of œstrone were begun shortly after birth. After eight months none of the surviving animals presented tumours, while in a similar period almost all of the mice of the strain previously studied had died of cancer of the breast. In the ninth month, however, the appearance of cancer was observed, and in the course of the following months others appeared, until by the 12th to the 18th month all the mice of this strain died of malignant tumours of the breast. The appearance of cancer was, therefore, only retarded in comparison with the other strain. Similar experiments upon mice in which spontaneous cancer never appeared in the ones surviving at 12 to 15 months showed that none of these had developed cancer of the breast.

Leo Loeb[8] states that the effect of hormones in the development of cancer is a specific one. A hormone influences the development of cancer only in those organs in which under normal conditions it has a specific relation, and only in cooperation with hereditary factors.

Loeb *et al.*,[9] experimenting upon a mouse the strain of which is relatively immune to cancer, began injecting it 18 days after birth. During the first eighteen months this animal got ten rat units of theelol in water daily; for the remaining six months daily injections of 30 R.U. of theelin. At autopsy the vagina, cervix and uterus were much enlarged. There were adhesions between the cervix and vagina and surrounding pelvic structures. Microscopic sections through the upper part of the vagina, cervix and uterus showed an extensive proliferation of squamous epithelium and pearl formation. The glands of the cervix and uterus showed active proliferation of epithelium with penetration into the deeper musculature. Loeb summarizes by stating that long, continuous application of œstrogenic hormones not accompanied by traumatization of the cervix may produce very far-reaching abnormal proliferations, not only in mammary gland but also in the vagina, cervix and uterus. The author states that if such pathological expressions were noticed in the human being they would have been called malignant. Hoffbauer[10] produced squamous metaplasia of cervical glands in mature guinea pigs by means of intraperitoneal injections of anterior pituitary substances from oxen and cows. He compared the condition to a healing erosion, but regarded it as precancerous. He also saw typical hyperplastic endometritis. In reviewing the results of our own clinic, where recently larger doses of œstrogenic products have been used, abnormal reactive histological changes in cervix and uterine epithelium would lead me to use œstrogenic products very carefully.

THE IRRITATION THEORY

This theory is best studied from the statistical reports. Dr. McFarlane[11] states that among the unsolved problems in connection with cancer of the uterus was the relationship which existed between the lacerations of childbirth and the development of cancer of the cervix. Approaching the subject from the clinical standpoint, she had reviewed hospital histories of 3,000 women, and from this series it appears that cancer of the cervix occurred six times as often in married parous women as in married nulliparæ. The question whether the increased incidence was due to lacerations predisposing to inflammations of the cervix or whether it was due to hormonal influences attending the pregnancy remained unanswered. A comparative study of Cæsarean section cases is required. In our clinic during the last ten years we have had cancer of the cervix occurring in the following proportions: multiparæ 88.7 per cent; married nulliparæ 7.3 per cent; and unmarried nulliparæ 4.2 per cent. Hunner, of Baltimore, states that in nearly 3,000 cases of endocervicitis with erosion treated by cauterization or amputation, during a 10-year follow-up not a single case showed carcinoma. My own daily histological inspection of these tissues over a period of fifteen years does not lead me to believe that laceration or erosion has any specific etiological bearing on cancer of the cervix. I strongly emphasize the neuro-vascular irritation theory with unbalanced tissue relations.

THE NEURO-VASCULAR IRRITATION THEORY

Cells growing from the human ovum have certain inherent characteristics: (1) capacity to grow and regenerate; (2) specialization, or differentiation, into tissues; (3) structural and functional coordination to organ and organismic entities. According to the modern conception of pathology cells are not looked upon as independently functioning bodies, but rather as a part of a relative system whose movements are dictated or modified by cell connections to, and contact with, each other, their stroma, blood vessels, and nerves (Oertel[12]). Cancers do not grow by this physiological scheme but by an abbreviated scheme overgrowing normal stationary tissues, as shown one hundred years ago by Thiersch and Waldeyer. According to the neuro-vascular theory an incoordination develops between plasma, blood vessels and nerves. Long-continued irritation, such as chronic inflammation, interferes with the normal tissue arrangement and constitution. Retrogression of tissues after the menopause, thrombosis in the capillaries of granulation tissue resulting in abnormal oxidation, abnormal growth and stimulation of nerves may lead to a permanent dilatation in capillaries, and if permanently prolonged irreparable damage to the contractile function of blood vessels with resulting hyperæmia is seen. This hyperæmia results in overgrowth of cells, loss of coordinated functioning, hyperplasias, metaplasias, and, if continued in this direction, loss of coordinated relationship of blood vessels, stroma, and nerves to each other.

Certain well known experiments should be mentioned at this time. The first of these con-

cerns microscopic observation of the nerve apparatus of the stomach in peptic ulcer by Stohr.[13] He demonstrated for the first time the finer nerve changes in and around gastric ulcers and showed an increase in the nerve processes in Auerbach's and Meissner's plexus, with considerable augmentation in the axis cylinders and Schwann's cells. Lymphoid-cell infiltrations were also found in the nerve plexuses. The ganglion cells were much changed with neuro-fibrillar outflow and hydrops. The nerve bundles proceeded in a spiral course of their cylinders into the ulcer granulation tissue and finally were lost in hypertrophic glandular masses. Scherer[14] has made observations which strongly point to a causal connection of nerves and nerve lesions with abnormal growth in a case of neuro-fibromatosis involving the œsophagus and stomach. Oertel has demonstrated in cancerous tumours, plexus and network formations of the advancing axis cylinders which deviate from the normal. When we consider cancers of the cervical portio which comprise about 85 per cent of the uterine cancers, and also that sub-epithelial nerve ganglia are only seen in the portio and lower cervical glandular region, not in the body of the uterus, as shown by Davies, we must seriously consider the neuro-vascular irritation theory where laceration, tuberculosis, syphilis, and erosion could upset, and bring about, an unbalanced coordination between the fixed tissues, nerves, and blood vessels, resulting in abnormal hyperæmia, overproduction of cells, hyperplasias, metaplasias, and go on into the abnormal cancerous growths. It would seem that by cauterization or amputation of the portio destruction of the subepithelial nerve plexus occurs, interfering with this neuro-vascular irritation. An etiological study of cancer of the cervix does not, therefore, give us reliable evidence. Our evidence leads us to consider a transformation in chromosomes; a change in cell relationship, transformation of normal cells into fractious ones. The true nature of this change will only be solved by a slow, intensive penetration into the laws which govern growth.

One of the main weapons against cancer, therefore, is a clinical ability to diagnose early in order to ensure favourable prognosis. Our responsibility as clinicians is great. A ready knowledge of associated or confusing pathological conditions of the cervix is imperative. Let us rehearse these confusing pathological diseases, namely, erosions, syphilis, tuberculosis, and leukoplakia.

Erosion is a dermatological term meaning desquamation or denudation of squamous epithelium. Any agent which denudes squamous epithalium creates erosion. About 90 per cent of erosions of the portio are bacterial in origin. A few follow digestive action of the menstrual fluid; a few represent endometriosis. One must clearly differentiate loss of squamous epithelium from that reddish, soft, hypertrophic growth of epithelium of the portio which often occurs in early pregnancy and follows in the puerperium. The healing of erosions follows a definite orderly sequence. The first stage of repair which represents the downgrowth of hypertrophic columnar epithelium over the denuded area may present an exaggerated expression of repair—papillary growth on the surface. These fine papillary projections present macroscopically a soft, red, velvety surface which if traumatized bleed easily because they are constructed of poorly bound, immature connective tissue, rich in exuded cells and small peripheral capillaries. This lesion simulates the rich, cellular, poorly organized, hæmorrhagic tissue of cancer. The second and third stages of healing of erosion are less confusing in their appearance, therefore will not be described in detail.

Tuberculosis of the cervix is a very rare pathological lesion. I have only seen one case of primary tuberculosis of the cervix in our clinic during the last ten years. Usually the lesion is part of the uterine one descending from the endometrium through the isthmus to the cervical canal. It may be part of a miliary tuberculosis. It may also accompany and overlie erosion of the cervix. Not always is there a soft greyish ulcer with serpiginous edges, but a hard, raised nodule, or even a polypoid growth, may extend downward from the portio resembling a carcinomatous growth. A microscopic study will show tubercles with giant cells lying in a partially necrotic granulation tissue.

Syphilis of the portio is more common than tuberculosis. The spirochæte most likely enters through a fissure, laceration, or erosion. Syphilis of the portio occurs primarily in three states: (1) a broad condylomatous ulcer like an ulcerating erosion; (2) syphilis of the portio associated with malignancy; (3) sclerosis of the portio, producing a hard, raised, indurated, inelastic growth growing from above downward. This state can easily be confused with the hard, in-

durating, intrinsic growth of squamous carcinoma. A microscopic view reveals a mature connective tissue with plasma cells, lymphocytes, and numerous thick-walled, sclerosed blood vessels lying in the deeper layers. About 8 per cent of all hard, sclerosed cervices will have a syphilitic origin. Secondary syphilis of the portio manifests itself in the form of macular, or papular eruptions, while tertiary lues of the portio is seen as gummatous growths, often kidney-shaped, with hard, underlying borders and a speckled grey, ulcerated centre. Microscopic section shows plasma cells and lymphocytes lying in a granulation tissue, with giant cells, which possibly are endothelial in origin. Below this one sees thick-walled, sclerosed blood vessels.

Leukoplakia of the cervix is becoming more frequent. The pathological nature of leukoplakia of the cervix must not be confused with leukoplakia of the vulva where about 30 per cent of all leukoplakias become malignant (Kearns[15]). Leukoplakia of the cervix is not a degenerative process as it is in the vulva, but rather an over-regeneration in squamous epithelium, or hyperkeratosis, as is frequently seen in prolapsed cervices with traumatized portios. It is also seen in the third stage healing of erosion, and in cases of long, continued œstrogenic medication. Rarely does leukoplakia of the cervix become malignant, even though large, irregular, thick strips or small polypoid projections of hyperplastic squamous epithelium are seen. I have seen leukoplakia of the portio frequently diagnosed as cancer, especially so since the introduction of œstrogenic medication.

METHODS OF TREATMENT AND RESULTS

The improved technique of radium treatment under proper screening and proper calculation of dosage has given us in our clinic immeasurable comfort. Rarely is it necessary to reradiate or treat necrosis or the after effects of over-radiation. Our concern chiefly has to do with prognosis. Prognosis is guarded by careful, regular follow-up examinations, and in the course of ten years we have only lost trace of one patient. For a careful follow-up a knowledge of the lymphatic drainage of the genitalia is imperative. A fundal carcinoma must travel through long, tortuous lymphatics in the wall of the uterus before reaching the first station in the parametrium, while a portio cancer has less distance to travel before involving the primary station, but an intrinsic cervical canal cancer has a comparatively short, direct course to involve the first station. The second, or promontory station, collectively takes in sacral, iliac, and hypogastric glands into one common regional station. The third station is half way between the superior and inferior mesenteric arteries, while the fourth station underlies the diaphragm.[16] These stations are not involved in a regular consecutive fashion, as was explained by Wertheim.

The results of treatment of cancer of the cervix in our clinic can best be presented by classifying our cases over a definite period of time into (1) the stages of malignancy; (2) the age of the patient; (3) the method of treatment. We have adopted the League of Nations Cancer Commission classification (1928). The first stage represents a growth in the cylinder of the cervix, a soft reddish, friable growth with or without limitations to the circumference of the canal. The second stage represents a growth which has extended from the surface through the full depth of the cervix musculature. The cervix and uterus are still mobile. In the third stage the growth has extended from the cylinder through the musculature of the cervix and has infiltrated the immediate attachments of the uterus such as the transverse parametria, the utero-sacrals, or the pubo-cervical fascia. The cervix and uterus are fixed by exudate in the pelvic fascia. The fourth stage represents involvement of surrounding structures as bowel, bladder, vagina, or pelvic lymph glands. The uterus and cervix are definitely fixed. Fistulæ may be present. Our material presented by stages is shown in the following tables.

TABLE I.

MATERIAL PRESENTING BY STAGES

Stages	*1*	*2*	*3*	*4*
Cases (total 68).....	6	10	38	14
Absolute salvage (total 20)	3	5	10	2
	50%	50%	26.3%	14.2%
Cases (total 63).....	6	9	37	11
Relative salvage (total 20) (radium-treated only)...	3	5	10	2
	50%	55.5%	27.02%	18.1%

Total salvage of all stages..... 29.4%

TABLE II.

CARCINOMA OF THE CERVIX
AUGUST, 1926, TO DECEMBER, 1936

Stages of Disease	*1*	*2*	*3*	*4*
Number of cases	31	57	188	51
	9.4%	17.4%	57.7%	15.5%
Total number of cases			327	
Parous			290	88.7%
Nulliparous			37	11.3%
Incidence of disease: Ages	20-30	30-40	40-50	50-
Number of cases	4	83	116	124
	1.2%	25.3%	33.4%	37.9%

I am grateful to Dr. Bauld and Dr. Percival for help in compiling this report; to Miss B. Stewart, R.N., our radium technician and statistician; and to Mr. W. J. Plumpton, technician, for the preparation of slides shown at the presentation of this paper.

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THE MANAGEMENT OF DIABETES MELLITUS BY THE GENERAL PRACTITIONER*

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FROM our standpoint as medical practitioners the treatment of diabetic patients covers at least four chief considerations. (1) Determination in each case of the optimum dietetic requirements—with or without insulin. (2) The care of minor or major disabilities or complications. (3) The treatment of coma. (4) The early diagnosis and treatment of peripheral vascular disease.

Since the discovery of insulin and its general use, and with what has been learned about diet, personal hygiene, the serious potentiality of many minor infections, as well as the life-saving methods applicable to coma, the young diabetics seldom die, the older patients have many years added, but eventually incur or succumb to degenerative arteriosclerotic disease. Indeed the early diagnosis and care of this phase of the diabetes often constitutes the major problem if they are to continue in health, comfort and usefulness. It is a truism that no one who has an apparently controlled diabetes can "travel alone". Careful medical supervision, with intelligent personal cooperation, is a *sine qua non*.

The doctor, alone, can, if given the opportunity, evaluate deviations from health, and institute early and proper measures for their control. There is scarcely any chronic disorder in which a happy outlook on life is more important, and it is clearly our duty to inculcate a cheerful philosophy with a background of care in our earliest contacts.

Glycosuria is, of course, not necessarily diabetes, but diabetes must be considered if sugar is found in a patient's urine. This is particularly true during pregnancy or upon its accidental discovery, when the other usual symptoms of diabetes are absent. If the blood sugar is taken two hours after a heavy meal and is over 140 mg. a glucose test should be done. If it be over 160 a diagnosis of diabetes may be considered established.

Delay in the control of glycosuria results in increased bodily damage, particularly if acetone bodies are present along with the urinary sugar. It also means a less liberal diet than may be eventually allowable and the use of insulin that might have otherwise been avoided. This delay

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is very undesirable and often is particularly difficult to overtake in adults. Their symptoms are often so mild, while the fear of a strict diet, or an unfounded belief in the necessarily permanent use of insulin, once begun, are so great that months and years of chronic disease may result. The effects of chronic dehydration, tissue injury through mineral and vitamin deficiency, and metabolic disease, predispose to serious or even irreparable vascular injury, infection or coma. It is likely that the periods of poor control, rather than the duration or severity of the disease, increase the incidence of serious complications.

No unanimity exists regarding the best type of diet, but recent tendencies incline to a more liberal allowance of carbohydrates. Regardless of the type to be used, many basic principles are similar. At commencement use one of very low caloric value, and increase slowly with manifest clinical improvement. The patient should be in bed for a few days while the food is being unduly restricted. The measurement and composition of the meals should be carefully taught. Increase of food should be made slowly each day until the required amount is given. This is determined by maintenance of the desired weight with freedom from abnormal fatigue, a feeling of well-being, and other evidence of control of the disease. Insulin must be given if the case is severe. Instruction must be given regarding its use, the control of mild reactions, and the technique of urinalysis. The occurrence of severe reactions or of unduly persistent glycosuria should always be avoided.

Mild cases are easily treated at home, frequently without interruption of the usual occupation. They require only moderate restriction of carbohydrate, fat, or both. Other types do better if treated in hospital. They do better because they have no responsibility in the preparation of their food, their new environment instils the necessity for care and accuracy, they are freed from minor worries and responsibilities of home or business, and they receive better education in their diet, insulin treatment and proper personal control of their disease.

If treated at home the patient should be put to bed for the first few days. The diet is slowly increased each day as long as the 24 hour urine shows an absence or only a trace of sugar. If sugar persists insulin is required. This should only be started when about 1,400 to 1,500 calories are given. The required amount is ascertained by testing with Benedict's solution at 8 a.m., noon, and at dinner time. With a red urine give 22 units, yellow 18, and green 10, at any of these periods. This is continued for another day or so; then the total daily insulin is divided into two doses, slightly more being given in the morning dose. Daily increases in diet then follow with enough insulin to maintain proper sugar control. The patient meanwhile is being taught the necessary details of self-care just as if he were in a hospital.

If desired the patient may be placed on protamine zinc insulin at any stage when control has been secured with regular insulin. Two-thirds of the daily insulin requirement is given as protamine zinc insulin and the remaining third as regular insulin an hour or half an hour before breakfast. The regular insulin is decreased and the protamine increased until a single dose of protamine only is given. This usually takes three or four days at least. Most diabetics requiring over 40 units daily need a combination of the two insulins, the regular being from 20 to 50 per cent of the protamine dose.

Protamine zinc insulin is a great advance in insulin therapy, but is potentially dangerous. It is slowly absorbed, acts for 36 to 48 hours, produces in the evening hours a slowly dropping blood sugar, frequently reaching abnormally low levels without any signs of hypoglycæmia even after many hours' duration. Reactions occur during these hours and are often different from those of regular insulin. Headache, nausea, vomiting or other gastro-intestinal symptoms are usual. When treated early in the evening with sugar they may recur, because the original dose of protamine is still acting. The earlier in the evening the reactions, the greater must be the amount of sugar given to prevent these symptoms. If the urine is still sugar-free, three hours later give more sugar, or food in the form of milk and a few crackers.

After a patient becomes controlled, it is most important to insist on daily urinalysis and a decrease of five or six units each day as long as urine sugar is absent. This is particularly important in cases requiring larger amounts of insulin. The dosage of regular insulin is the first reduced, since one tries to ultimately use a single injection, that of the protamine.

Severe cases require some regular insulin given by a separate injection at the same time as that of protamine, to control the rapid absorption of sugar taken in the regular meals,

while the protamine controls the nocturnal tendency to hyperglycæmia. Overdoses of the regular insulin produce reactions during the day time. These commonly occur in the mornings and are often controlled in severe cases, in children, or adults in active occupations, by giving an apple or its equivalent about ten-thirty in the morning. Clinical control is usual if there is a trace of sugar in the urine at 6 p.m. and if the 8 a.m. specimen is sugar-free with no feeling of headache. Reduction of both doses (protamine and regular insulin) is necessary to avoid serious reactions if specimens at these hours are sugar-free. A small night lunch on retiring of crackers, milk, cheese or its equivalent, as well as the three regular meals and the 10.30 apple, is easily arranged if the diet is the type that contains 150 to 200 grams of carbohydrate.

The patient may be considered under good control if his diet is adequate, if he maintains his weight at the desired level with a feeling of vigour and little fatigue, if he is free from reactions, if his fasting blood-sugar is under 160 mg. per cent, if his weekly 24 hour urinalysis usually indicates freedom from sugar and acetone, and if his knowledge of personal hygiene is carefully followed. Despite modern laboratory investigation, his clinical state is still of the greatest importance to the observant physician. Practically, it is safer to allow occasional slight glycosuria and the feeling of health that results than to strive for consistently normal blood-sugars and risk reactions or the feeling of fatigue that may ensue. This also applies clinically to certain patients who have a high renal threshold (hyperglycæmia but no glycosuria) and who feel well.

After a few weeks, when exercise, food requirement, insulin dosage are harmoniously adjusted, a period of stability ensues. This is interrupted during the succeeding months and years when the incidental strains of living are intensified. Diabetics often respond abnormally to these factors. Emotional episodes, worries, fears, infections, minor and major—in short, illness of all sorts, medical, surgical or obstetrical, provoke exaggerated symptoms of the illness or of the diabetes. If the diabetes is controlled, the ultimate response of complications to treatment is almost as good as in any other patient. It is the uncontrolled diabetic that is always the poor risk.

It is during this period of normal good health, often laboriously attained, that carelessness usually develops. One must see his patient at least every six weeks. The addition of extra food, of extra supply of vitamins, particularly the "B complex", the use of extra salt, calcium, or the treatment indicated for complicating diseases are all frequently necessary. The patient should be examined for changes in the vascular system, heart, eyes and feet. Early treatment of these defects is most profitable.

Acidosis usually develops when relatively minor symptoms are neglected, commonly, loss of appetite, vomiting, infectious fevers or diarrhœa. Insulin, if being taken, must on no account be stopped, and should be given every four hours in sufficiently large doses to control gross glycosuria. Food is taken as fluids, and extra fluid given to the point of tolerance. As the malady subsides soft food of the previous dietary content is substituted, the insulin requirement divided into two doses, continuing until the original diet in solid form can be taken. Mild acidosis when neglected may suddenly become aggravated and true diabetic coma result. These cases are medical emergencies and must be so treated. Dehydration, loss of sodium chloride and other minerals, the cardio-renal damage from toxæmia or the complicating infections require prompt energetic treatment. Forty or sixty units of insulin are given at once, depending on the depth of the coma. Glucose in saline, with 20 to 50 units of insulin, well mixed, is given intravenously. I personally prefer to give about 2 litres of 5 per cent glucose, 25 units of insulin per litre, in normal saline, running the solution at about 400 to 500 c.c. per hour. The urine should be collected by an indwelling catheter and tested every three hours. The insulin dose depends on the amount of sugar present. External warmth, enemata, stomach lavage, circulatory stimulants, as well as other symptomatic treatment, are necessary. At least 3,000 c.c. of fluid should be given daily by mouth when possible, by duodenal tube, intravenously, or interstitially, containing plenty of salt and at least 150 to 200 g. of glucose. Sufficient insulin is given to control extreme glycosuria and avoid reactions. Five or six doses are usually required the first day or so. The size of the dose and its frequency depends on the age of the patient, weight, depth of coma, its untreated duration, and the presence or absence of infection. These measures are more

efficiently managed in hospital. Additional assistance is there available, through a knowledge of the CO_2-combining power, the non-protein nitrogen, and sugar content of the blood at various times. There also the patient is more quickly returned to the previous diet and stabilized with insulin. Excellent results, however, are obtainable in the home with the help of competent nurses and assistants.

Careful inquiry and examination will frequently discover early vascular impairment of the legs and feet. Crampy pains in the calf muscles, paræsthesia, burning sensations over the toes, dorsum or heel, usually worse at night, chronically cold feet, absence of hair and perspiration, distorted, discoloured nails, atrophic skin and muscles, with various degrees of impaired pulsation in the arteries all indicate the progress of the arterial thickening that always exists with diabetes. In the early stages of arterial change there is minor disability. Progression is unceasing and the trouble is very great later. The feet should be kept warm, thick woollen stockings being worn night and day. Extreme care is necessary in avoiding blisters from new boots, trauma in trimming corns or the nails, or accidental injury, and unduly long walks, particularly in cold weather, should be avoided. Massage, warm sitz baths before retiring, and various types of mild sedatives give sound sleep in the more troublesome cases. Several patients have been found to benefit from properly applied diathermy and short wave, from high vitamin therapy, particularly that of the "B complex", from increased sodium chloride intake, and from a course of a hundred hours in the Pavaex boot.

The onset of the next episode may be delayed for years by skilful prophylactic treatment, but is inexorable. A trifling, superficial injury, sometimes a forgotten one, results in superficial thrombosis, gangrene or, worst of all, infection. This requires absolute rest in bed, comfortable elevation of the limb, and protection from rubbing and from irritating bed clothing. It is presumed, of course, that the diabetes has always been controlled. Local treatment should be mild, *e.g.*, boracic or cod liver oil ointment, balsam of Peru, dry dressings, with alcohol-cleansing daily. Superficial infections are treated with weak eusol, avoiding sogginess of surrounding tissue. Here again various types of physiotherapy and local applications are of value. Staphylococcus toxoid may be used, commencing with small doses and increasing every five days until 0.5 c.c. is given. The basic principles are rest, conservation of body heat, symptomatic treatment, and surgical measures before they are too late. In applying any treatment one must remember that the tissues are injured by chronic metabolic disease and an inadequate blood supply. Consequently, repair of any injury, thermal, traumatic or chemical, is slow, and the inability to localize damage or infection leads to rapid and widespread damage.

Infections may be treated as in other surgical cases, particularly if, as often happens, the patient is a younger adult with slightly damaged arteries. In older patients, or if the infection is not localizing, if high fever, toxæmia, and increasing glycosuria are evident, it is dangerous to delay a safe operation and risk a blood-stream infection. The exact procedure in this type of case requires careful surgical and medical teamwork to produce the best results, in saving life, in conserving a limb, or even in expectant treatment.

Space forbids further consideration of the surgical or pregnant diabetic. Both complications should be safe if one controls them before the event. Neither affords a contraindication, and neither will aggravate the disease. Glycosuria discovered in pregnancy is usually non-diabetic.

In conclusion may I suggest that the moderately severe diabetic should be hospitalized as soon as possible. In hospital instructions regarding the disease minimize damage from complications. The alert physician further lessens the effects of complications by early and energetic treatment. The problem of proper safeguards during the years of added life is approximated by no other disease, and requires the patient to have the complete cooperation and vigilance of a sympathetic and intelligent adviser in the person of the family physician.

In the short period allotted one regrets the inability to be more detailed in the consideration of these problems. The conclusions offered represent personal experiences. The publications of many interested in this work have been freely used in the preparation of this paper, and their valuable assistance is gratefully acknowledged.

FORS CLAVIGERA IN ANÆSTHESIA*

BY WESLEY BOURNE

Montreal

THERE is not less wit nor less invention in applying rightly a thought one finds in a book than in being the first author of that thought. Thus wrote Peter Bayle in 1696, giving many illustrious examples and likening the opposite to a foolish affectation never to quote anybody, and to fetch everything from home; like that Ælian Hippias who merrily boasted all he had about him was his own handiwork. Emerson, too, has said that by necessity, by proclivity, and by delight, we all quote. Thus it is that I do not hesitate to borrow from Ruskin his *Fors Clavigera,* and copy his meanings of these words out of a desire to present some observations in a desultory and accidental manner.

Fors is the best part of three good English words — force, fortitude, and fortune; hence "the first", "the second", or "the third Fors". Concerning *Clavigera,* we have the meanings from *clava,* a club, *clavis,* a key, and *clavus,* a nail, or a rudder; and from *gero,* I carry. This is the root of our word "gesture"; and in a curious bye-way, of "jest". Putting these together, one finds: Fors, the Club-bearer, the strength of Hercules, or of Deed; Fors, the Key-bearer, the strength of Ulysses, or of Patience; and Fors, the Nail-bearer, the strength of Lycurgus, or of Law (rule of any kind). With such appositeness, therefore, it is proposed to discuss discursively some more or less recent deed in anæsthesia; vagrantly, to tell a little of the fortitude of the workers in the field; and, cursorily, to touch upon a few cogent rules in the orderings of relevant fortune.

Properly to suage the throes of fear before anæsthesia not nearly enough is being done. Metaphysical principles should be applied more regularly, that is, some psychological ritual ought to be carried out and cooperated in by all those attending a case. Reassurance should be given by calmative statements and gestures. Then, and then only, sedative drugs should be administered, in doses much larger than is customary. A good practice is to give repeated doses until the desired effect is attained. For healthy adults I prefer to administer ¼ gr. of morphine and 1/100 gr. scopolamine 75 minutes before the time of operation and repeat the same in about 45 minutes if the patient is not thoroughly well subdued and in a state of complete indifference. It is advisable to use smaller doses in the very old, whereas with children relatively larger quantities may be employed with advantage, as has been shown by Robson, of the Sick Children's Hospital of Toronto. The most important reason for increased pre-medication is the removal of fear. The apprehensive person will all too often become severely shocked, particularly in spinal or other forms of regional anæsthesia, in whom, if sedation is complete, there will be much less fall in blood pressure than otherwise, no nausea, and a salutary degree of amnesia. During regional anæsthesia the patient does well to be, as it were, oblivious, in the Cimmerian cave. Again, in general anæsthesia, by how much the more sedative drugs are used by so much the more readily will narcosis be induced and maintained. Someone will say that such heroic doses may interfere with respiration or circulation, or both. The answer is that after considerable experience I have yet to see disturbance, and Waters, of the University of Wisconsin, who has been making observations on the subject with even larger doses, informs me that there are: "little if any change in oxygen consumption, decreased minute volume with morphine alone, a slight increase with scopolamine alone, and distinctly less reduction in the minute volume with the combination. . . . Pulse changes tended toward an increase with morphine and no increase, or even a decrease, with scopolamine". These findings constitute an example of real synergism. When it is desirable to use avertin then this drug takes the place of morphine in general anæsthesia, and atropine only may be given with it. A word or two about the barbiturates will suffice. Generally speaking, as preliminary medicaments in surgery they are not to be compared with morphine, on account of the likelihood of immoderate excitement and delayed action. In obstetrics, however, Mac-

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Phail, Gray and I have shown, at St. Mary's Hospital, Montreal, that pentothal, a *sulphur* barbiturate, is perhaps the most suitable substance for the earlier suffering of labour.

Undoubtedly the most recent cynosure in anæsthesia is that which came from those anchorites of the pharmacological laboratory of Toronto University, Henderson and Lucas, and was introduced clinically by Waters and his coworkers at the University of Wisconsin, I mean cyclopropane. This gas is being used so extensively, especially in hospital practice, that in several instances it has completely replaced ether; indeed, it has been said that, but for purposes of teaching, ether would not be given in many places. Nevertheless, one must constantly remember its great potency and administer it slowly in low concentration. It might be likened to basil, which when "softly touched yieldeth a sweet scent, but chafed in the hand, a rank savour." The two significant features about cyclopropane anæsthesia are that it usually produces adequate relaxation, and an abundance of oxygen may be given with it. This latter constitutes its special suitability in obstetrics. Raginsky and I have shown that cyclopropane anæsthesia under the most strenuous of circumstances does no harm to the liver.

A new ether has been brought forward by Leake and his collaborators, of the University of California, and studied by several others, notably Guedel, of California, Goldschmidt and Ravdin with their collaborators, of the University of Pennsylvania, and Molitor, of the Research Laboratories of Merck & Co. This material, vinyl ether, produces insensibility very rapidly and is recovered from equally so. It is therefore particularly useful for intermittent administration in obstetrics by general practitioners, or those who, from lack of experience, may not give cyclopropane. Vinyl ether has been recommended in minor surgery and for short dental operations. It is no more toxic than ethyl ether, and Raginsky and I have proved that the effects of each on the normal or impaired liver are practically equal. The employment of vinyl ether is increasing, but it is still somewhat difficult to obtain.

To return to regional anæsthesia; that form devised by Etherington-Wilson, of Torquay in England, is found to be exceedingly satisfactory, chiefly when complete relaxation is required, and, too, for chest surgery. The technique consists in injecting a percaine solution into the spinal canal while the patient is sitting. The solution, 1 in 1,500, is lighter than spinal fluid and rises at a constant rate, so that with some slight variation, which depends on the length of the spinal column, the sitting posture is maintained during 20 to 30 seconds for operations below the umbilicus, during 30 to 45 seconds for those of the upper abdomen, and during 45 to 60 seconds for surgical procedures on the chest. Surgeons universally, express their contentment with the ease of operating when there is complete muscular relaxation, particularly in the upper abdomen. Fraser Gurd, Arthur Vineberg and I, at the Grace Dart Home Hospital in Montreal, after trying all forms of anæsthesia in thoracic surgery, have found the method of Etherington-Wilson to be the best from all points of view. We have attained a good *dénouement* in the subject. It seems to be at its acme, if for two reasons only; namely, there is so little bleeding during the operation, and the post-operative course is nearly always without concern, in antithesis to that of all other modes of anæsthesia in this type of surgery. Although this method of spinal anæsthesia is very appealing and is carried out with great despatch, yet beginners are warned to develop considerable dexterity with it for operations below the umbilicus before daring to go further. It may be pointed out at this time that the good results obtained are in large measure due to the profound depression of the cerebral cortex by large doses of morphine and scopolamine as mentioned earlier in this paper.

Now for a consideration of analeptics. It is my firm belief that they should not be used as a routine, nor in anticipation of shock. They tend to stimulate the central nervous system. Raginsky and I have shown that ephedrine reverses the effects of avertin, and will undo the desired and purposely produced depressant actions just stated. Further, it is known that stimulating drugs may cause untoward results when used in normal beings; there are several instances of this. It is better to observe carefully the blood pressure and its relation to the pulse rate, and then, only when there is sufficient alarm, should analeptics be administered. Melville, of the Department of Pharmacology of McGill University, has shown a remarkable synergism between ephedrine and the pressor principle of posterior pituitary extract. Each of these substances alone will produce a rise in blood pressure in a shocked individual, but in

each the rise is transient and a severely shocked animal will go on to die. Now, if less than half quantities of these two substances are given together the pressure will rise, often above what it was in the first place, and will so stay up that the animal lives. Recently, in 79 spinal anæsthesias, 60 for abdominal operations and 19 for thoracic operations, O'Shaughnessy and I, at St. Mary's Hospital and the Grace Dart Home Hospital, Montreal, have satisfied ourselves clinically of the efficacy of these two drugs in restoring the circulation after serious depression.

The penultimate topic of this discourse is carbon dioxide, than which there is no more abused chemical in medicine, and it took Waters to disclose the truth, Ralph M. Waters, than whom there is no more forceful worker in the vineyard of interdepartmental cooperation—the laboratory and the clinic. One of Paul's portraits may apply to him: "blameless, . . . vigilant, sober, of good behaviour, apt to teach, . . . not greedy of filthy lucre". These are the attributes of the scientist, yet one remembers the grievous words pronounced by Fourquier-Tinville at the trial in which Lavoisier was condemned to the guillotine; "The Republic has no need for Scientists". In similitude, with more dissembling, how true is this even now! But let us with Carlyle say: "The public is an old woman. Let her maunder and mumble." But let us gon on with carbon dioxide. Last June, at Ottawa, before this Section, Waters discussed carbon dioxide in a syncretistic manner, showed that it may produce convulsions, that surgical shock is not the result of low CO_2 in the blood and tissues; that anæsthesia does not cause a lowering of the CO_2 content of the blood and tissues; that post-operative pulmonary atelectasis is not necessarily prevented by CO_2 and oxygen; and that CO_2 is a waste product of body metabolism, just as are the constituents of urine. These results were given despite the expoundings of Yandell Henderson. Waters advises never to apply CO_2 therapy or rebreathing to prevent or ameliorate shock. Simple oxygen treatment is more satisfactory. During anæsthesia he avoids dead space and rebreathing as much as as possible. He removes the CO_2 of the expired air with soda-lime. He uses CO_2 solely as an analeptic when it is desirable to accomplish rapid elimination of toxic volatile gases, and then a small stream of pure CO_2 is directed towards the face. From a physiological point of view these teachings seem to be quite sound and worthy of reiteration.

Oxygen has just been mentioned, and we do well to remember that it is the vitally important constituent of air, and that discouragement of its use in the treatment of pulmonary diseases was due to the fact that it was, in the early days, administered neither properly nor early enough. Now, thanks to the pertinacity of such men as Geoffrey Bourne, of London, England, John Evans, of Buffalo, N.Y., and Alvan Barach, of New York City, the benefits of the administration of oxygen are universally recognized. Goldschmidt and Ravdin, of the University of Pennsylvania, and Raginsky and I have often demonstrated the dangers of anoxia during anæsthesia, as well as their alleviation by oxygen. We do well to remember, too, that oxygen is virtually a food; indeed, in anæsthesia it might be considered an ambrosial food, supplying the blood and tissues with their requirements at a time when obstructions to breathing may occur, and preventing or lessening what might be serious changes in vital functions.

In this most strenuous of Iron Ages, when vicissitudes seem continually to increase, the anæsthetist must carry his share with courage and patience, while seeking rules beside the Fates. In conclusion, therefore, and as a further apologia, to say the truth, one cannot but be impressed with Ruskin's title. He tells us, "My own conception of it was first got from Horace". The worthy Rabbinic principle, "Say a thing in the name of the man who said it", and proverbs will remain maxims; witness those of Balthasar Gracian, like unto *Application and Ability, Man of Rectitude,* and *Fortune and Fame.*

ADMINISTRATION OF HORMONES. — Deanesly and Parkes have investigated experimentally the effectiveness of crystalline gonadal hormones when administered by the subcutaneous implantation of solid tablets of the pure substance. The technique is particularly useful when a long-continued steady effect is required, as, for example, in the depression of the gonad-stimulating and growth-promoting activity of the pituitary by œstrogens, and in the masculinization of the female by androgens. Treatment of very long duration following one administration of hormone will apparently be possible by this method of implantation.—*The Lancet*, 1938, **2**: 606.

THE RESULTS OF PHRENIC NERVE PARALYSIS IN THE TREATMENT OF PULMONARY TUBERCULOSIS*

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THIS review will probably add little to the now existent voluminous literature on the subject of phrenic nerve paralysis in the treatment of pulmonary tuberculosis. However, as the exact value of the procedure and its indications are still controversial, we feel that our experiences with it are worthy of record.

As is quite well known to all those having care of the tuberculous sick, phrenic operations were very widely used some years ago, with rather disappointing results when taken as a whole. Such has been the history of a great many operations, until experience has shown just where and when they should be used; the exact indications once being established, their value remains undisputed. It has been so with phrenic paralysis. At first there was a widespread enthusiasm with inclusion of cases we now know should not be treated by this means. This of course could be followed by but one attitude of mind—skepticism, but from this experience emerges a knowledge of true values. Many of the early cases herein reported would not today have been advised to have this type of therapy and many more who received a permanent paralysis would have had a temporary one. Unfortunately, we have to report our group as a whole, but we hope and believe that the results of the operation during the next few years will be more gratifying than they have been in the past.

With one exception, we are now doing more phrenic operations at the Nova Scotia Sanatorium than any other institution in Canada, and we feel justified. It is not intended, however, to give the impression that we are using them in an attempt to avoid the major procedure of thoracoplasty, or as a trial method, as more thoracoplasty operations are done than phrenics. We attempt to evaluate each case on its own merits and apply whichever procedure seems best.

From personal communication with all the sanatoria of Canada we were somewhat surprised to learn that in many of the institutions so few cases are being treated by this procedure. Table I indicates the number of cases and percentages treated by operative measures in the various sanatoria during 1937. Institutions are indicated by number only, but all are tuberculosis sanatoria. By referring to column 4 it will be seen that the number of patients receiving a phrenic paralysis in 1937 was rather meagre.

It is to be observed from this table that phrenic nerve paralysis is not generally employed in Canadian sanatoria to the extent that it appears to be warranted as an aid in the treatment of pulmonary tuberculosis. Why this should be is not easy to explain. Perhaps we have become accustomed to use pneumothorax over a long period of time, even in those cases where a phrenic operation would do just as well, in spite of the fact that 70 to 80 per cent of pneumothoraces are followed by effusions of mild or serious nature, and of these 15 to 18 per cent become purulent, requiring thoracoplasty. Perhaps the original results of phrenics were so discouraging that some institutions have hesitated to re-apply the procedure. Perhaps the operations have been faulty, leaving behind accessory fibres with a resultant poor paralysis or early return of function, or an adequate surgical service may not be at hand. There may be a number of reasons, but at any rate, the general attitude seems somewhat different from our own. Again we do not wish to give the impression that we are advising phrenic operations in place of pneumothoraces. Each has its own definite indications, but in cases where a phrenic will probably produce as good a result as a pneumothorax, we feel that the patient is subjected to

* Read before the Canadian Medical Association Meeting, Halifax, N.S., June 22, 1938.

less danger of complications and relieved of the burden and expense of pneumothorax maintenance.

There is probably no branch of surgery in which it is more difficult to set down indications and contraindications for a certain type of operation than in the surgical treatment of pulmonary tuberculosis. However, we will briefly outline the conditions under which we now consider phrenic operations of value and also where we feel that they should not be used.

They are particularly suited for early unilateral lesions with soft infiltrative changes in the upper or lower lobes of the lung. In these cases, we believe that they are about as effective a procedure as pneumothorax and less troublesome of application, and certainly less expensive to the patient. Small, thin-walled, cavities of a diameter of less than 3 cm., with a surrounding infiltration capable of contraction, deserve a trial of a temporary phrenic paralysis before pneumothorax is started. If successful the length of paralysis can be prolonged by a second operation, and if unsuccessful a pneumothorax can be added without serious loss of time. There are many cases in which collapse therapy is indicated where a pneumothorax is impossible on account of adhesive pleuritis. In these a phrenic should be done, provided a thoracoplasty or extra-pleural pneumothorax is not definitely indicated. It is usually the method of choice in the treatment of basal lesions in which pneumothorax is impossible or ineffective. In our institution it is frequently used where it is impossible for the patient to carry on pneumothorax treatment at home. It is frequently of great value as a supplementary measure to re-expansion after prolonged pneumothorax treatment. Its value in the control of certain cases of hæmoptysis is well recognized.

There are a considerable number of patients who complain of persistent cough and chest pain as a result of traction from a lung adherent to the diaphragm or even of traction at the apex. The relief by a phrenic paralysis in these cases is very gratifying to the patient even if there exists no necessity for extra collapse for control of the disease.

TABLE I.

SURGICAL PROCEDURES IN USE IN CANADIAN SANATORIA

TABLE SHOWING THE NUMBER AND PERCENTAGE OF PATIENTS IN WHOM DIFFERENT TYPES OF OPERATIVE PROCEDURE WERE EMPLOYED DURING THE YEAR 1937

Institution	*Number of patients treated*	*Pneumothorax*		*Pneumolysis*		*Phrenic paralysis*		*Thoracoplasty*	
		No.	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*
1	139	24	17.0	0	..	0	..	0	..
2	356	73	20.5	3	0.8	0	0	4	1.1
3	143	84	58.7	0	..	22	15.3	7	4.9
4	216	109	50.5	0	0	37	17.1	6	2.8
5	223	104	46.7	0	..	18	8.0	5	2.2
6	302	59	19.5	1	0.3	13	4.3	14	4.6
7	1,234	232	18.8	10	0.8	22	1.7	28	2.2
8	424	59	13.9	0	..	3	0.7	3	0.7
9	182	32	17.5	0	..	0	..	0	..
10	190	53	27.8	0	..	0	..	0	..
11	418	177	42.3	9	2.1	5	1.2	8	1.9
12	1,160	168	15.0	12	1.0	16	1.5	9	0.8
13	419	193	46.1	..	..	20	4.7	89	21.3
14	179	76	42.5	0	0	8	4.5	11	6.1
15	715	231	32.3	7	1.0	16	2.2	0	0
16	544	170	31.2	39	7.1	51	9.4	33	6.1
17	107	29	27.1	0	..	3	2.7	2	1.8
18	....	..	40.0	..	3.4	..	21.0	..	6.0
19	306	97	31.7	11	3.6	1	0.3	6	1.9
20	185	54	29.2	0	0	2	1.1	0	0
21	847	407	48.0	40	4.7	22	2.3	46	5.4
22	376	196	53.0	29	7.7	20	5.3	25	6.6
23	531	82	15.4	3	0.6	4	0.8	30	5.7
24	215	46	21.4	0	..	0	..	4	1.9
25	884	97	10.9	8	0.9	80	9.0	34	3.8
26	567	201	35.5	42	7.4	7	1.2	33	5.8
Total...	10,862	3,053	38.1	214	2.0	370	3.4	397	3.6

"No." at the head of each of the last four columns refers to "Number of operative measures carried out".

Little benefit can be expected from the operation in those cases where thick-walled cavities exist. From our tables to follow it will be noted that not a single thick-walled cavity was closed by the procedure. Cavities larger than 4 cm. in diameter are seldom obliterated by this measure alone. The operation is not indicated in those cases in which the cavity is peripherally located and held open by adherent pleura, nor is multiple cavitation ordinarily helped to any great extent. Advancing lesions of an active exudative type are seldom benefited. It is the opinion at our institution that a phrenic operation should never be used when a thoracoplasty is definitely indicated, as a trial method, nor should it be used as a preliminary to thoracoplasty. There are several reasons for this. In the first place we feel that when a patient comes to thoracoplasty he should have his maximum of vital capacity. Secondly, although there is much experimental evidence to show that a patient may more effectively clear his lower lobes of secretions immediately after paralysis of the hemi-diaphragm it would appear this does not hold true after several months of paralysis. It has been our experience at any rate that basal spreads are far more frequent after thoracoplasty in those cases with a paralyzed diaphragm than in those with a functioning one. Thirdly, it is also believed that if a patient is to be subjected to any type of permanent collapse therapy he should be left with as much functioning lung and as high a vital capacity as possible. Even a phrenic operation designed to be only temporary does not always permit return of function, and so it is quite possible to rob a patient of good lung and considerable vital capacity. There are cases in which the disease is active, soft and infiltrative, where an immediate thoracoplasty cannot be done, but where a temporary phrenic operation will render the patient suitable in a few months for that procedure.

In regard to the type of operation, we now believe that the paralysis produced should be temporary rather than permanent, except in a comparatively few cases. In our own series of 250 cases (up to 1937, however) only 61, or 24.4 per cent, had temporary phrenic paralysis, while 189, or 75.6 per cent, were of the permanent type. We have regretted the permanency of the paralysis in many instances. Some of those who needed thoracoplasty had basal spreads following the operation, and the treatment of subsequent contra-lateral disease is decidedly complicated by a permanent diaphragmatic paralysis on the opposite side. It is safe to say that all operative procedures should be so planned as to preserve as much good lung as possible and to leave the patient with his maximum vital capacity.

Our first temporary operations consisted only of crushing the nerve. This we found unsatisfactory, in view of the fact that diaphragmatic function returned far too early for the procedure to be of any great value. We are now dividing the main trunk and suturing it with fine silk, then hunting for all accessories and dividing them. This procedure we have found to be more satisfactory. It is very important that all accessories be found and divided or a very poor result will be obtained.

Phrenic operations were first done at the Nova Scotia Sanatorium, in 1930 and from then until 1937 were used 250 times. The early cases were practically all exeresis, and before the establishment of a surgical service at the institution many rather far advanced cases were included, which today would at once be subjected to thoracoplasty. The results therefore, are possibly not so gratifying as they might have been.

It may not be amiss to mention that a carefully prepared questionnaire was sent out early in 1938 to all our patients who had undergone phrenic operations and we were able to account for all patients except one. Through the cooperation of the Department of the Public Health, Halifax, we were able to gain exact information as to the cause of death in those who have succumbed. All x-ray films were read and commented upon by our radiologist, while the patients' records were carefully analyzed by a trained chartist.

The study herein is presented under the following headings: (1) Sex and age, (2) Stage of disease at time of operation, (3) Types of disease and lobes involved, (4) Types of operations employed, (5) Complementary measures used, (6) Results on tubercle bacilli in sputum, (7) Results on cavity closure, (8) Operative accidents and complications, (9) Causes of death, (10) Present condition of all patients.

Of the 250 patients, 97, or 38.8 per cent, were males and 153, or 61.2 per cent, females. Their ages are listed in Table II.

TABLE II.

Ages	*Number*	*Percentage*
10 to 19	36	14.4
20 to 29	127	50.8
30 to 39	55	22.0
40 to 49	20	8.0
50 to 59	10	4.0
60 to 69	2	0.8
Total	250	100%

The greatest number, 77.8 per cent, who had had phrenic paralysis were adults between the ages of 20 to 40. The oldest, a man of 69, a far-advanced case of tuberculosis, was distinctly benefited as a result of the operation. Within a very short time the distressing cough, which had troubled him for many months, was greatly relieved, and his sputum reduced considerably in amount. Chest pains at the base of the affected lung were also much improved.

The stage of the disease at the time of operation is indicated in Table III.

TABLE III.

STAGES OF DISEASE

Stage	*Number*	*Percentage*	*Total*	*Percentage*
Minimal:				
Unilateral	15	6.0		
Bilateral	3	1.2	18	7.2
Moderately advanced:				
Unilateral	21	8.4		
Bilateral	39	15.6	60	24.0
Far advanced:				
Unilateral	27	10.0		
Bilateral	145	58.0	172	68.8
Total	250	100.0	250 or	100.0

Here it is seen that 232, or 92 per cent of these patients, were either in the moderately advanced or far advanced stage of tuberculosis, while 18, or 7.2 per cent, were in the minimal stage.

As in the majority of institutions in America we admit patients to the Nova Scotia Sanatorium in all stages of tuberculosis. Fully 70 per cent on arrival are already far advanced. We have, therefore, to select cases for compression therapy as well as we can, under circumstances over which we have no control. While some of these cases at first may not appear to be ideally suited for hemi-diaphragmatic paralysis, we are often agreeably surprised, even in bilateral lesions, when phrenic paralysis is employed, either as an independent measure or combined with some other operative aid. The indications and contraindications have been briefly outlined above, along with a comment on the type of operations used.

In Table IV it is seen that the operation was used both independently and in combination with other methods of collapse therapy. When used in combination it is rather difficult to evaluate the merits of each procedure, but, as O'Brien pointed out in one of his articles, this is as it should be. The object is to close the lesion and render the sputum free from bacilli.

TABLE IV.

	Number	*Percentage*
Phrenic alone	126	50.4
Phrenic+Px.	72	28.8
Phrenic+Px.+Pneumolysis	10	4.0
Phrenic+Px.+Thoracoplasty	14	5.6
Phrenic+Thoracoplasty	18	7.2
Phrenic+Oleothorax	7	2.8
Phrenic+Oleothorax+Thoracoplasty	3	1.2
Total	250	100.0

From the public health viewpoint the rendering of a positive sputum to one free of tubercle bacilli is the most important function of any type of therapy. The results in our series were as follows.

TABLE V.

RESULTS OF PHRENIC PARALYSIS ON TUBERCLE BACILLI

A. Phrenic paralysis alone	*Number*	*Percentage*
Patients with tubercle bacilli before operation	65	
Patients without tubercle bacilli after operation	26	40.0
B. Phrenic paralysis combined with other operative aids		
Patients with tubercle bacilli before operation	79	
Patients without tubercle bacilli after operation	47	59.5

From the patient's viewpoint the arrest of disease and the closure of cavities is most important. The results of phrenic paralysis alone and phrenic paralysis combined with other procedure on cavity closure is indicated in Table VI, parts I and II.

Of the 177 cavities treated by phrenic paralysis, either alone or combined with other operative aids, 63, or 35.6 per cent, were closed and 40, or 23.2 per cent, decreased in size. In other words, 58.8 per cent of all patients definitely benefited by this procedure. It was

TABLE VI.

RESULTS OF PHRENIC PARALYSIS ON CAVITIES ACCORDING TO LOCATION, NUMBER, SIZE AND TYPE

I. RESULTS OF PHRENIC PARALYSIS ALONE ON CAVITIES

Location of cavity	*Number*	*Closed*	*Decreased*	*Stationary*	*Larger*
R_1	34	9 (26.5%)	8 (23.5%)	2 (5.9%)	15 (47.1%)
R_2	8	1 (12.5%)	2 (25%)	1 (12.5%)	4 (50%)
R_3	8	4 (50%)	3 (37.5%)	0 (0%)	1 (12.5%)
L_1	32	7 (21.9%)	8 (25%)	9 (28.1%)	8 (25%)
L_2	8	4 (50%)	1 (12.5%)	1 (12.5%)	2 (25%)
Total..	90	25 (27.8%)	22 (24.4%)	13 (14.5%)	30 (33.3%)

II. RESULTS OF PHRENIC PARALYSIS COMBINED WITH OTHER OPERATIVE MEASURES ON CAVITIES

Location of cavity	*Number*	*Closed*	*Decreased*	*Stationary*	*Larger*
R_1	28	8 (28.6%)	8 (28.6%)	3 (10.7%)	9 (32.1%)
R_2	9	3 (33.3%)	1 (11.1%)	1 (11.1%)	4 (44.5%)
R_3	9	6 (66.7%)	2 (22.2%)	0 (0%)	1 (11.1%)
L_1	30	12 (40%)	7 (23.3%)	5 (16.7%)	6 (20%)
L_2	11	9 (81.8%)	1 (9.1%)	1 (9.1%)	0 (0%)
Total..	87	38 (43.7%)	19 (21.8%)	10 (11.5%)	20 (23%)

R_1 = Right upper lobe. R_2 = Right middle lobe.
R_3 = Right lower lobe. L_1 = Left upper lobe.
L_1 = Left lower lobe.

observed that lower lobe cavities were much more likely to be obliterated or diminished than were those situated in the upper lobes. When other operative aids were brought to the assistance of the diaphragmatic paralysis it was seen that 88.9 to 90.9 per cent of basal cavities were closed or made smaller.

By referring to part I of the Table it is seen that 27.8 per cent of all cavities were obliterated by means of phrenic paralysis alone. When other operative measures were added (part II) it is seen that 43.7 per cent were closed. This confirms our impression that when a cavity is not closed or decreased in size within a reasonable period of time, probably three months, following a phrenic operation, we should not delay in instituting other operative procedures such as artificial pneumothorax, thoracoplasty, or extra pleural pneumothorax in an attempt to bring about a satisfactory result.

An analysis was made of the results of the operations according to the size of the cavity. These results are set forth in Tables VII and VIII.

TABLE VII.

RESULTS OF PHRENIC PARALYSIS ALONE ACCORDING TO SIZE OF CAVITIES

A. Total cavities greater than 3 cm.....	34
Number closed.....	3 or 8.8%
Number decreased in size.....	11 or 41.2%
Number stationary or larger in size....	20 or 58.8%
B. Total cavities less than 3.1 cm.....	56
Number closed.....	22 or 39.3%
Number decreased in size.....	11 or 19.6%
Number stationary or larger in size....	23 or 41.1%

TABLE VIII.

RESULTS OF PHRENIC PARALYSIS COMBINED WITH OTHER OPERATIVE MEASURES, ACCORDING TO SIZE OF CAVITIES

A. Total cavities greater than 3 cm.....	40
Number closed.....	16 or 40.0%
Number decreased in size.....	11 or 27.5%
Number stationary or larger in size....	13 or 32.5%
B. Total cavities less than 3.0 cm.....	47
Number closed.....	22 or 46.8%
Number decreased in size.....	8 or 17.0%
Number stationary or larger in size....	17 or 36.2%

By reference to the size of cavities we note that phrenic nerve paralysis alone is of little value when the diameter of a cavity is greater than 3.0 cm. Only 8.8 per cent of such cavities were obliterated. When this procedure was combined with additional surgical aids 40 per cent of these larger cavities were closed, which is a result comparable to that obtained in the case of the smaller cavities (6.8 per cent less).

We may say that as the diameter of a cavity increases its chances of closure by phrenic paralysis alone decrease. If other operative measures are also used the size of the cavity has not the same prognostic value. No doubt many of the cavities which remained open after diaphragmatic paralysis would have been closed had it been possible to offer the patient the benefit of a thoracoplasty operation, which unfortunately was not available at the sanatorium during the early years of this study.

Whether or not cavity closure can be expected as a result of the operation depends

largely upon the state or type of the cavity wall. The results of the operation alone, or combined, are shown in Tables IX and X.

RESULTS OF PHRENIC PARALYSIS ON CAVITIES ACCORDING TO LOCATION, NUMBER, SIZE AND TYPE

TABLE IX.

RESULTS OF PHRENIC PARALYSIS ALONE ON DIFFERENT TYPES OF CAVITIES

Character of walls	*Number*	*Closed*	*Decreased*	*Stationary*	*Larger*
Thin....	19	7 (36.8%)	7 (36.8%)	3 (15.8%)	2 (10.6%)
Mod. thick..	26	10 (38.5%)	7 (26.9%)	5 (19.2%)	4 (15.4%)
Thick...	13	0 (0%)	1 (7.7%)	2 (15.4%)	10 (76.9%)
Consolidation	21	8 (38.1%)	3 (14.3%)	2 (9.5%)	8 (38.1%)
Total..	79	25 (31.6%)	18 (22.8%)	12 (15.2%)	24 (30.4%)

TABLE X.

RESULTS OF PHRENIC PARALYSIS COMBINED WITH OTHER OPERATIVE MEASURES ON DIFFERENT TYPES OF CAVITIES

Character of walls	*Number*	*Closed*	*Decreased*	*Stationary*	*Larger*
Thin....	15	8 (53.3%)	2 (13.3%)	1 (8.8%)	4 (26.6%)
Mod. thick..	24	12 (50%)	3 (12.5%)	2 (8.3%)	7 (29.2%)
Thick...	20	5 (25%)	7 (35%)	3 (15%)	5 (25%)
Consolidation	19	8 (42.1%)	6 (31.5%)	4 (21.1%)	1 (5.3%)
Total..	78	33 (42.3%)	18 (23.1%)	10 (12.8%)	17 (21.8%)

It is interesting to note from Tables IX and X that phrenic nerve operations alone were not successful in closing thick-walled cavities and caused only one such cavity to decrease in size. Thin and moderately thick-walled cavities, as well as those occurring within areas of pneumonic consolidation, appear to respond to treatment uniformly; 36 to 38 per cent of cavities in these classes were obliterated as a result of this procedure.

We may now point out that although fully 91 per cent of thick-walled cavities failed to improve from the phrenic paralysis alone, indeed, 76.9 per cent increased in size, yet when other operative procedures were combined with the phrenic nerve operations it was found that the chances of closing thick-walled cavities were greatly increased, about one out of four being entirely obliterated. The results of phrenic paralysis, when used alone, on the various types of disease is shown in Table XI.

TABLE XI.

RESULTS OF PHRENIC PARALYSIS ALONE ACCORDING TO TYPE OF DISEASE

A. WITH CAVITIES

	Exudative	*Mixed exudative-productive*	*Productive*
Apparently cured.....	5 (9.1%)	8 (34.8%)	1 (100%)
Arrested and apparently arrested	7 (12.7%)	4 (17.4%)	0 (0%)
Improved.....	15 (27.3%)	3 (13%)	0 (0%)
Stationary.....	4 (7.3%)	1 (4.4%)	0 (0%)
Worse.....	4 (7.3%)	0 (0%)	0 (0%)
Dead.....	20 (36.3%)	7 (30.4%)	0 (0%)
Total..... 79	55 (69.6%)	23 (29.1%)	1 (1.3%)

B. WITHOUT CAVITIES

	Exudative	*Mixed exudative-productive*	*Productive*
Apparently cured.....	4 (20%)	2 (7.7%)	1 (100%)
Arrested and apparently arrested	10 (50%)	17 (65.4%)	0 (0%)
Improved.....	5 (25%)	4 (15.4%)	0 (0%)
Stationary.....	1 (5%)	1 (3.8%)	0 (0%)
Worse.....	0 (0%)	0 (0%)	0 (0%)
Dead.....	0 (0%)	2 (7.7%)	0 (0%)
Total..... 47	20 (42.6%)	26 (55.3%)	1 (2.1%)

When the prognosis is considered in the light of the type of disease present it is found that there is surprisingly little variation whether the disease be exudative or mixed exudative-productive (Table XIB). When cavity formation exists, however (Table XIA), it is seen the chances for recovery are greatly lessened

and the better results are obtained when the disease is of the mixed exudative-productive type. It is noteworthy that only four cases were not improved, arrested, or apparently cured when the original disease was free from cavitation.

Comparatively few operative accidents occurred in our series of the 250 cases. One female had a Horner's syndrome. The paralysis lasted for almost a year, and then gradually cleared up. In another case there was moderate bleeding during the extraction of the nerve. This was controlled with hot packs, and lasted but a few minutes. We have had no deaths as a result of phrenic exeresis. Nor have we come across any of the serious accidents reported from time to time in the literature. Post-operative complications in the majority of our cases were of a minor nature. There was one patient who had a contralateral spread of the disease. This did not occur until a month following the operation and might well be attributed to the natural course of the disease. There were two cases of severe dyspnœa following left-sided phrenic paralysis, in one of which there was difficulty also in the matter of defæcation. The dyspnœa in both instances slowly subsided within a period of two months. There were also several cases of dyspnœa of a transient nature lasting from a few days to a few weeks. A small number of patients complained of digestive symptoms, with flatulence and pyrosis. These manifestations lasted but a brief time.

In five of cases of the number which eventually came to thoracoplasty there was rather marked basal spread following the first-stage operation, which delayed a second operation for some time. In these five it was felt at the time that the basal spread would probably not have occurred had the diaphragm not been high and fixed and incapable of transmitting the cough pressure impulse from the abdomen to the lung base. All were of long-standing, and the nerves, of course, had been avulsed. Possibly such basal spreads can be called a late complication of the phrenic and as much blame placed upon it as on the thoracoplasty. If the diaphragm is still resilient enough to yield with a pressure impulse from the abdomen basal spreads are not so apt to occur. This latter state of affairs exists in more recent phrenic operations where the diaphragmatic muscle is not yet completely atrophied and fibrosed.

Of the 250 patients 54 are now dead. Through the courtesy of the Department of the Public Health, Halifax, we have been able to determine the causes of death among the 250 cases reported (1930-37).

TABLE XII.

Cause of deaths	*Number*
Asthenia—progressive disease	37
Cardio-respiratory failure	2
Post-operative, following thoracoplasty	5
Post-operative, following thoracoplasty—spontaneous pneumothorax, contralateral lung	1
Tuberculous meningitis	1
Fatal hæmoptysis	4
Acute pneumonitis following inspiration of oil—broncho-pleural fistula	1
Spontaneous pneumothorax	1
Asthenia plus Pott's disease	1
Unknown	1
Total	54

It is seen from the above table that all have died as a direct result of their disease either by extension or complications. There were no deaths from causes other than tuberculosis.

The present condition of the whole group of 250 patients is seen by reference to Table XIII, parts I, II and III. These tables also include the groups from year to year, and are divided according to whether phrenic operation was used alone or in conjunction with other procedures.

It is seen that when the operation was used alone that of the 126 patients so treated 21, or 16.7 per cent, are apparently cured; 37, or 29.4 per cent, are arrested; 27, or 21.4 per cent, are improved; 8, or 6.3 per cent, are stationary; 4, or 3.2 per cent, are worse; 29, or 23 per cent, are dead, and all are accounted for. In going up the scale from improved to cured we find there were 85 of the 126, or 67.3 per cent, in this group.

In the group of 250 cases 124 patients received phrenic combined with other types of collapse therapy. In this group the results are somewhat better. Of these 29, or 23.4 per cent, are apparently cured; 28, or 22.5 per cent, arrested; 28, or 22.5 per cent, improved; 5, or 5.0 per cent, stationary; 8, or 6.6 per cent, worse; 25, or 20.2 per cent, are dead; and the condition of one is unknown.

When the group is considered as a whole 50, or 20 per cent, are aparently cured; 65, or 26 per cent, arrested or apparently arrested; 55, or 22 per cent, improved, 13 or 5.2 per cent, sta-

TABLE XIII.

I. PRESENT CONDITION OF 126 PATIENTS
TREATED BY PHRENIC PARALYSIS ALONE
DURING THE EIGHT-YEAR PERIOD, 1930-1937, INCLUSIVE

Condition in 1938	*Year of operation and time elapsed*								*Total*
	1930 or Eight years ago	*1931 or Seven years ago*	*1932 or Six years ago*	*1933 or Five years ago*	*1934 or Four years ago*	*1935 or Three years ago*	*1936 or Two years ago*	*1937 or One year ago*	*1930-37 Up to eight years*
Apparently cured	1	5	4	5	1	3	2	0	21 = 16.7%
Arrested and apparently arrested	0	2	0	0	3	6	20	6	37 = 29.4%
Improved	0	1	0	1	1	5	7	12	27 = 21.4%
Stationary	0	0	0	0	1	2	0	5	8 = 6.3%
Worse	0	1	0	1	0	0	2	0	4 = 3.2%
Dead	3	8	4	5	4	4	1	0	29 = 23.0%
Unknown	0	0	0	0	0	0	0	0	0 = 0.0%
Total	4	17	8	12	10	20	32	23	126 = 100.0%

II. PRESENT CONDITION OF 124 PATIENTS
TREATED BY PHRENIC PARALYSIS COMBINED WITH OTHER COMPLEMENTARY MEASURES
DURING THE EIGHT-YEAR PERIOD, 1930-1937, INCLUSIVE

Condition in 1938	*Year of operation and time elapsed*								*Total*
	1930 or Eight years ago	*1931 or Seven years ago*	*1932 or Six years ago*	*1933 or Five years ago*	*1934 or Four years ago*	*1935 or Three years ago*	*1936 or Two years ago*	*1937 or One year ago*	*1930-37 Up to eight years*
Apparently cured	5	7	8	4	2	2	1	0	29 = 23.4%
Arrested and apparently arrested	0	3	1	3	3	4	10	4	28 = 22.5%
Improved	1	4	0	3	3	5	6	6	28 = 22.5%
Stationary	0	0	0	1	0	0	3	1	5 = 4.0%
Worse	2	1	1	1	0	0	1	2	8 = 6.6%
Dead	4	5	1	6	2	3	4	0	25 = 20.2%
Unknown	0	0	0	0	1	0	0	0	1 = 0.8%
Total	12	20	11	18	11	14	25	13	124 = 100.0%

III. PRESENT CONDITION OF 250 PATIENTS
TREATED BY PHRENIC PARALYSIS*
DURING THE EIGHT-YEAR PERIOD, 1930-1937, INCLUSIVE

Condition in 1938	*Year of operation and time elapsed*								*Total*
	1930 or Eight years ago	*1931 or Seven years ago*	*1932 or Six years ago*	*1933 or Five years ago*	*1934 or Four years ago*	*1935 or Three years ago*	*1936 or Two years ago*	*1937 or One year ago*	*1930-37 Up to eight years*
Apparently cured	6	12	12	9	3	5	3	0	50 = 20.0%
Arrested and apparently arrested	0	5	1	3	6	10	30	10	65 = 26.0%
Improved	1	5	0	4	4	10	13	18	55 = 22.0%
Stationary	0	0	0	1	1	2	3	6	13 = 5.2%
Worse	2	2	1	2	0	0	3	2	12 = 4.8%
Dead	7	13	5	11	6	7	5	0	54 = 21.6%
Unknown	0	0	0	0	1	0	0	0	1 = 0.4%
Total	16	37	19	30	21	34	57	36	250 = 100.0%

*Either alone or with other complementary measures.

tionary; 12, or 4.8 per cent, are worse; 54, or 21.6 per cent, are dead; and one is unknown. It is seen that of the whole group 68 per cent are improved or better than that.

SUMMARY AND CONCLUSIONS

1. A brief discussion of phrenic paralysis operations is given.

2. The extent to which the operation is used in Canada is indicated. It would appear that it is not employed so widely as seems justified in carefully selected cases of tuberculosis.

3. The indications and contraindications are briefly discussed.

4. It is recommended that in the vast majority of cases the temporary operation rather than the permanent one should be used.

5. An analysis of 250 cases is given.

We wish to express our thanks to Dr. J. Earle Hiltz, assistant superintendent, who reviewed all x-ray films and prepared a number of the tables for us; to Dr. C. J. W. Beckwith, D.M.H.O., Cape Breton, for assistance rendered in the early years of our phrenic work; also to Mr. Allen d'Entremont who studied the case histories and charted the material therein, and conducted the follow-up on these patients.

BLOOD-CULTURE AS AN AID TO THE DIAGNOSIS OF CARCINOMA AND SARCOMA*

BY O. C. GRUNER, M.D.

Montreal

THE occurrence of bacteria in neoplastic tissue is generally recognized, and is usually ascribed to local infection in the case of ulcerated growths, and to coincidence in the case of other neoplasms. In other words, the tumour tissue is regarded as a form of culture medium to which organisms are particularly attracted whenever they enter the blood stream. It has however to be admitted that bacteria are seldom numerous enough in cancer tissues to be seen by direct histological examination of sections.

Various workers, notably Doyen (1902), Schmidt (1903), Glover (1920), Nuzum (1921), Young (1921), Stearn (1929) and Aaser (1934) have approached the subject of cancer bacteriology as a problem in etiology, since, of course, clinical bacteriology starts out from the concept that certain bacteria specifically account for certain diseases. In the absence of convincing evidence to the contrary, the organism successively described in relation to cancer by the above-named and other workers continues to be regarded by many authorities as belonging to the category of secondary invaders or of coincidental and non-significant associates.

In the present communication the notions "causation" and "infections" are purposely avoided, for, indeed, the validity of those concepts is disputable in any case. It is simply a record of the findings in blood-cultures which have been taken routinely both in proved cancer cases and in suspected cases. The only point of interest has been to ascertain whether there is or is not a particular kind of bacterial flora in the blood of cancer patients which would enable a diagnosis to be made in difficult cases.

In a preliminary series of 104 proved cases of malignant disease, studied between 1933 and 1938, various routine media and mycological media were employed, using a pH from 7.0 to 7.6. The Kimble broth culture tube (60021, pH 7.4) was finally preferred. Growths were always scanty, even after subculture, except in the case of cryptomyces which grew readily after adaptation. The following results were obtained:

TABLE I.

Name of organism	*No. of cases*
Doyen micrococcus*	52
San Felice organism	6
Cryptomyces	17
Organisms other than these	19
Negative result	10

* This corresponds to the Glover organism of Table II.

During the past nine months, using the empty Kimble tube (60016), it has been possible to collect blood from nearly every case of cancer coming into the Royal Victoria and Montreal General Hospitals.* By this means all risk of contamination of the blood is done away with.

* This work was made possible by a grant from the Archibald Cancer Research Fund, McGill University.

* By the valuable cooperation of Drs. Morton and Raymond, respectively.

METHOD OF OBTAINING THE PRIMARY CULTURE

After sterilizing the skin of the forearm and drawing up the blood according to the instructions provided in the cartons (Kimble Glass Company, Chicago) the tube is shaken vigorously at short intervals for about five minutes. In this way the blood will continue to remain fluid. After standing overnight at room temperature, some 5 c.c. of the blood are introduced into one or more tubes of Glover's agar medium, prepared strictly according to the instructions published in the *Canada Lancet and Practitioner*, 1930, **74**: 92, and verbally explained by Dr. Murray Wright, of Philadelphia, whose guidance is here gratefully acknowledged. The pH of this medium is 6.5.

CULTURAL FINDINGS

The organism found in this series presented the characters described in the publication mentioned above, so that details need not be given here. Pyogenic cocci, streptococci, coliforms, Salmonellas, non-pathogenic sporogenes and others were all excluded by reason of the distinctive features of the Glover organism, namely, inability to obtain good primary cultures on other media, very slow development, peculiar steel-blue tint to the naked eye after 48 to 72 hours, distinctive motility, distinctive odour, non-fermentation of lactose, absence of gas formation on any sugars, filterability through Chamberland and Seitz filters.

RESULTS

The second series comprises 347 cases. Of these 152 were proved malignant (carcinoma, sarcoma); 56 others were definitely not cancer. The remainder are not yet utilizable, either because the diagnosis is not final or because the culture results are not fully available.

In the following table, "positive" means that besides the typical organisms an easily visible growth was obtained; "equivocal" means that though the organisms were found, there was only a very faint visible growth; "negative" means that neither macroscopic nor microscopic growth could be found after fourteen days' incubation.

TABLE II.

Cancer cases	*No. of cases*	*Cultural result* — *Positive*	*Equivocal*	*Quite negative*
Before treatment started	19	14	2	3
Treated by surgery or radiation*				
Still under treatment	24	21	2	1
Treatment ended				
6 months ago or less	35	28	1	6
6 to 12 months ago	17	13	1	3
2 years ago	16	12	3	1
3 to 5 years ago	15	10	2	3
Over 5 years ago	3	3	–	–
Untreatable and inoperable	23	22	1	0
Total	152	123	12	17
Percentage positive		88		12
Non-cancer cases	56	2	–	54
Percentage positive		4		96

* Mostly deep x-ray therapy.

The table shows that the organism in question has been found in blood-cultures in 135 out of 152 proved cases of cancer (both treated and untreated), whereas only 2 out of 56 cases clinically free of cancer gave a positive result. This method of study therefore seems likely to be helpful in the diagnosis of obscure cases.

Confide not to thy friend every secret thou possessest; how knowest thou that he will not sometime become thy foe? Inflict not every injury thou canst upon an enemy; it is possible that one day he may become thy friend.—*Maxim IX* of the Sheik Sa'di of Shiraz.

Reveal not thy secret to any man although he may be trustworthy, because no one can keep thy secret better than thyself.

Silence is preferable than to tell thy mind to anyone, saying what should remain unsaid. O simpleton! Stop the source of the spring; when it becomes full the brook cannot be stopped.—*Maxim X* of the Sheik Sa'di of Shiraz.

THE BLOOD SEDIMENTATION RATE IN ANÆMIA

BY HAROLD SUGARMAN, M.D.

Saskatoon

IN view of some controversy as to the influence of anæmia on the blood-sedimentation rate, we analyzed the records of 177 cases of uncomplicated anæmias in which routine blood sedimentation rates were performed. Of these 167 were hypochromic anæmias, 9 pernicious anæmias and 1 aplastic anæmia. This analysis was confined to ambulatory office patients.

The blood sedimentation rate is valuable in all conditions as an aid in the differentiation between some active pathological process and a more innocent functional disturbance. It is also of value in determining the grade of activity of the disease. For the past two years we have used the test as a routine procedure, and have either found active disease in every case where the sedimentation rate was rapid, or made doubly sure our search was thorough, where none was located. A normal sedimentation rate does not exclude the presence of some disease process. The test is very simple, not time-consuming, and requires no laboratory facilities. It can be carried out at the patient's home as well as the physician's office or at the hospital. Several methods are used and we have found the following technique the most practical in routine work.

Apparatus.—1. Sedimentation tube (Cutler), 1 c.c. capacity, 5 mm. in diameter, marked in millimetres beginning with zero at the one c.c. level to 50 mm. at the bottom.

2. A one or two c.c. syringe, graduated in tenths and a hypodermic needle (sterile).

3. Several ounces of 3 per cent sodium citrate in normal saline or an aqueous solution of 3.8 per cent sodium citrate (sterile).

4. Tourniquet, alcohol and gauze sponges.

5. Graph paper (not essential).

Procedure.—Draw exactly 0.1 c.c. of the citrate solution into the syringe, and fill up to the 1 c.c. mark with blood from a prominent vein. Draw in a large bubble of air and tilt the syringe to mix the citrate with the blood to prevent clotting. Spurt the blood into the sedimentation tube up to the zero mark. The tube is kept perpendicular. Record the cell drop every ten minutes for the first half hour and again at the end of an hour.

The normal sedimentation rate varies from 2 to 10 mm. in one hour in men, and 2 to 15 mm. in one hour in women. The changes occurring in the first half hour are more significant.

Of 167 cases of uncomplicated hypochromic anæmias where no active disease process could be demonstrated only 4 had an increased sedimentation rate varying from 16 to 18 mm. in one hour; 163 had normal sedimentation rates, and of these only 16, all female, showed the maximum normal range from 10 to 15 mm. in one hour. The remaining 4 with increased sedimentation rates occurred with the following blood estimations: (1) Sedimentation rate of 18, hæmoglobin 57 per cent (Sahli), and red blood count, 4,100,000. (2) Sedimentation rate 17, hæmoglobin 65 per cent (Sahli) and red blood cell count 4,100,000. (3) Sedimentation rate 16, hæmoglobin 67 per cent (Sahli), and red cell blood count 4,800,000. (4) Sedimentation rate 16, hæmoglobin 65 per cent (Sahli) and red cell blood count 3,800,000.

The reduction of hæmoglobin to as low as 36 per cent (Sahli), where the red blood count was over 3,000,000 per c.mm., had no effect on the sedimentation rate. Where the red blood count varied from 3 to 5 million per c.mm. no significant or proportional change was found in the sedimentation rate.

In the hypochromic anæmias red blood counts below 3,000,000 per c.mm. were not encountered. Therefore, it appears from our analysis that a red blood count lower than 3,000,000 per c.mm. is not the rule with uncomplicated hypochromic anæmia and should be taken more seriously. Where a high-grade secondary anæmia with a red blood count below 3,000,000 did occur it was invariably secondary to a known complication such as an occult bleeding lesion, carcinoma, etc. In these the sedimentation rate was increased. This type of case is not included in this analysis.

In pernicious anæmia, however, we find a definite increase in the blood-sedimentation rate. Out of 9 cases examined where the blood-sedimentation rates were taken, 7 showed a sedimentation rate varying from 18 to 35 mm. in one hour. Two cases with red blood counts of 2,700,000 and 3,700,000 had sedimentation rates of 10 mm. and 8 mm. in one hour, respectively. In both of the latter cases the sedimentation rates were taken during a remission after the patients had been on treatment with

liver extract for some time. In each of the 7 cases, where the blood sedimentation rate was rapid it varied inversely with the number of red blood cells per c.mm. These ranged from 2,500,000 to 1,300,000 per c.mm. of blood, and the sedimentation rate varied accordingly from 18 mm. to 35 mm. in one hour. In one of the seven cases during a relapse, when the red blood count was 1,300,000 per c.mm., the sedimentation rate was 35 mm. in one hour; during a remission, when this patient had been under treatment and the red cell count came up to 2,500,000 the sedimentation rate was reduced to 15 mm. in one hour.

In 9 cases of pernicious anæmia, compared with 167 cases of hypochromic anæmia, we find that in pernicious anæmia the sedimentation rate is definitely increased during a relapse and tends to become normal during a remission.

One case of aplastic anæmia with a red blood count of 1,500,000 per c.mm. showed a sedimentation rate of 40 mm. in one hour.

CONCLUSIONS

1. In uncomplicated hypochromic anæmias the hæmoglobin percentage has no influence on the blood sedimentation rate. Where the red blood count is above 3,000,000 and up to 5,000,000 per c.mm. the sedimentation rate shows no corresponding variation.

2. A red cell blood count below 3,000,000 per c.mm. signifies the presence of some complication and should be taken more seriously.

3. In pernicious anæmias there is a definite increase in the blood-sedimentation rate during a relapse which tends to become normal during a remission. The lower the red cell count, the faster is the sedimentation rate.

I wish to thank Dr. D. M. Baltzan for the privilege to make this analysis and the supervision in preparing this report.

ABERRANT RENAL VESSELS*

(REPORT OF TWO CASES)

BY G. A. WINFIELD, M.D.

Halifax, N.S.

I WISH to present two cases of aberrant renal vessels, both occurring in males, and both causing acute symptoms. In neither of these cases was there a marked hydronephrosis, and both were cured by simple ligation and division of the aberrant vessel.

CASE 1

This patient, a truck driver, thirty years of age, was first seen on March 24, 1937. He complained of pain in the back, on the left side, and blood in the urine. The complaint dated back four months, and previous to that time he had never had any trouble. While driving his truck he had a sudden severe pain in the left side, over the left kidney, and referred along the course of the left ureter. The pain was severe enough to require morphine for its relief. From that time on he had several attacks, considerably less in severity, but still quite severe. Frequently, after an attack of pain urination was accompanied by a burning sensation, and on several occasions he had seen blood in the urine. This had apparently not been sufficient to cause him any alarm.

On examination the patient appeared to be a robust white male, apparently in excellent health. The general physical examination was entirely normal. Examination of the genito-urinary system revealed the following positive findings. There was definite tenderness in the left loin, referred down the course of the left ureter. The kidney was not palpable. Urinalysis revealed a trace of albumin, with about 15 blood cells per high-power field. No pus or casts were seen. The white blood cells were 7,500. Cystoscopy was advised, and was carried out under caudal anæsthesia. The bladder appeared entirely normal. The right ureter was easily catheterized, but a catheter was obstructed in the upper portion of the left ureter. No urine appeared from the left side. Indigo-carmine appeared from the right side in 4 minutes, in good concentration. No dye appeared from the left in 12 minutes.

Pyelograms revealed a moderate right hydronephrosis. The left ureter was visualized to the level of the third lumbar vertebra, and was irregular at this point. The kidney outline appeared larger than normal. No dye entered the left pelvis.

In view of the history of bleeding, the absence of stone, and the x-ray findings, a tentative diagnosis of renal neoplasm was made, and an exploratory operation on the left kidney advised. This the patient refused, and left the hospital.

He returned four months later, stating that he had been perfectly well until the previous two weeks, when he had had another severe attack of left-sided pain. He had had no bleeding and no urinary symptoms. A cystoscopic check was advised, which the patient refused. He did consent, however, to an intravenous pyelogram, which revealed a functioning left kidney, and ruled out the diagnosis of neoplasm.

The two sets of plates were reviewed in comparison, and a provisional diagnosis of aberrant vessel made. At operation on August 4th, a small aberrant artery was found, arising from the renal artery, crossing behind the ureter just below the uretero-pelvic junction, and entering the lower pole of the kidney. The ureter was definitely kinked over this vessel. The artery was ligated and divided, after which the ureter was seen to straighten out. The kidney was in good position and was not disturbed.

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* A paper read at the Sixty-ninth Annual Meeting of the Canadian Medical Association, Section of Urology, June 23, 1938.

The patient made an uneventful recovery and left the hospital on the 11th day after operation. He has remained perfectly well to date.

CASE 2

The patient, a man of 24 years, entered hospital complaining of pain in the left side. Two months previously he had had an attack of severe pain in his left side. This was located in the region of the kidney and did not radiate. There was no nausea. The pain lasted an hour or so and then disappeared. The patient remained well until two weeks before his admission. He then had another milder attack, which lasted about an hour and a half. Twenty-four hours prior to admission, while walking, he was seized with a severe left-sided pain, located in the left loin and the left side of the abdomen. The pain was sharp, stabbing, and did not radiate. The patient was nauseated and vomited. Urination at this time was accompanied by slight burning. He went to bed, but was unable to sleep until his pain was relieved by morphine. The next day the pain again required morphine, and this did not relieve him. He was then ordered to hospital.

Upon examination he appeared to be in rather acute pain. He was rather stuporous, with a temperature of 97.4° and a cold skin. The pupils were pin-point, and it was evident that he had had large doses of morphine.

The abdomen showed no movement on respiration. The rectus on the left side was rigid and the abdomen extremely tender. The maximum tenderness was in the left costovertebral angle, extending downward. The left kidney was not palpable. The white blood cells numbered 8,500. The urine showed a trace of albumin, 15 pus and about 50 red blood cells per high-power field.

The clinical diagnosis was hydronephrosis due to ureteral stone. A plain plate was negative for calculus, and cystoscopy was done. The bladder was entirely normal except for some slight inflammation. Both ureteral orifices were normal and both were easily catheterized. There were a few red cells from each side, but no pus. Indigo-carmine appeared from the right side in ten minutes, and from the left in fifteen. Pyelograms were done, and revealed a normal right kidney, with a left hydronephrosis. A diagnosis of left aberrant renal vessel was made, and the patient operated upon.

At operation a small aberrant renal artery was discovered, coursing from the renal artery to the lower pole of the kidney. The ureter was kinked over the vessel, and showed considerable dilatation. The point of obstruction was just below the ureteropelvic junction. The vessel was divided between ligatures, after which the ureter was seen to straighten out. The patient made an uneventful recovery. An intravenous pyelogram, made two weeks after operation, showed moderate hydronephrosis on the left side. In comparison with previous films there was marked improvement in the appearance of the left kidney. This patient has remained well to date.

The first case of hydronephrosis due to an aberrant vessel was reported by Boogard in 1857. The patient died from an intestinal ailment, and at autopsy distension of the right renal pelvis was noted. There was an abnormal distribution of the renal artery which divided at its origin into branches, one of which went to the lower pole of the kidney. This branch crossed the ureter near its origin from the pelvis, causing definite compression of it. In 1894 Fenger devised an operation for the relief of this condition, reporting 5 cases with three clinical cures. In 1906 Duval, Gregoire, and others reported an excellent study of the rôle of aberrant vessels before the 10th session of the French Urological Association. In the past few years the condition has received considerable attention in the American literature, and a large number of cases have been reported.

A review of the literature indicates that the condition is not uncommon. Eisendrath and Strauss in an examination of over 1,200 kidneys found anomalous vessels present in some 21 per cent. Burr concurred with these findings, but stated that 80 per cent went to the upper pole, and hence caused no symptoms. Anomalous veins do not appear as commonly as anomalous arteries, but when associated with nephroptosis are just as important. The artery may or may not be accompanied by a vein, but the veins never occur alone. The vast majority of anomalous vessels cause no symptoms.

The condition occurs in early adult life, between the ages of 25 and 40, commonly. It is said to occur more often in females, and on the right side. The condition may be bilateral. Higgins, in a recent report of 52 cases, found the condition in 28 males and 24 females. The average age at the appearance of symptoms was 25. The oldest was 67; the youngest 9. In 80 per cent of cases symptoms occurred before the age of 40.

In 150 cases of hydronephrosis associated with nephroptosis, operated on by Mathé, 6.1 per cent had aberrant vessels causing kinking of the ureter. These included only those vessels going to the lower pole.

The presence of anomalous vessels is undoubtedly associated with embryological development. The embryonic kidney is rich in blood supply, and as it ascends to its normal position it receives its blood supply from higher and higher sources, discarding those from below as it progresses. Thus the anomalous vessels may be but the retention of a portion of the normal vascular relations of the embryo before the ascent of the mesenephros to the renal fossa. Mathé states that there may be from one to six vessels per side, depending on the number of vascular relations retained.

Various theories have been advanced to explain the manner in which hydronephrotic changes are produced. Three theories predominate: (*a*) The vessel crossing the ureter acts as an actual mechanical obstruction when associated with movable kidney or an infected kidney. The weight of the organ causes it to sag from its

normal position, the ureter being suspended over the vessel, with consequent kinking. (*b*) A mechanical obstruction is produced in the ureter at the point of contact with the vessel, resulting in adhesions and a consequent fixation of the ureter at that point. (*c*) Quinby maintains that the contact of the pulsating vessel interferes with ureteral peristalsis and hence with the normal emptying of the renal pelvis.

We believe that symptoms may and do occur before any great hydronephrosis is present, and it has not been our experience that renal ptosis is necessarily a factor. It must, of course, be remembered that the normal kidney is capable of some excursion.

Whatever theory one accepts, it must be conceded that there is some interference with normal drainage. This is the cause of the pain, and will result in hydronephrosis, which may be extremely large. In many advanced cases infection occurs, with abscess formation and possibly calculi, resulting often in a hopelessly damaged kidney. The symptoms as a rule are not severe, but acute attacks do occur. Pain is the outstanding feature, usually dull aching in character and definitely localized in the affected renal angle. It usually occurs in attacks, varying in frequency and, as time goes on, increasing in severity, with a decrease in the free period. The attacks often follow exercise, and are usually relieved by rest, especially in the Trendelenburg position. Menstruation and lying on the affected side intensify the pain. Nausea, vomiting, and perspiration are frequent accompanying symptoms, and may be misleading. The attacks usually last a few hours, and are followed by a dull non-radiating ache. It is interesting to note that the severity of the attack is no criterion of the amount of hydronephrosis present. Hæmaturia is frequently present, but usually late, when renal damage has occurred. This, however, was not true in case 1.

During an attack there is almost always tenderness in the affected costovertebral angle, and those cases in which the pelvic distension is great may present a palpable tumour. As a rule there are no urinary symptoms. Urinalysis is most commonly normal, but may reveal an occasional white and red cell. A trace of albumin in an otherwise normal urine is of some significance. The renal function estimated from the combined renal output is normal. A normal temperature and white blood count are characteristic, unless, of course, infection be present. The patient's general condition is, as a rule, excellent. Cystoscopy reveals a normal bladder. Occasionally the ureteral orifice on the affected side will show some retraction. Both ureters are easily catheterized. Differential renal function tests may show a diminution on the affected side.

Diagnosis.—Because of the varied and vague symptoms, frequently related to the gastro-intestinal tract, the diagnosis may be easily missed. The chief point is to keep the condition in mind. Any young adult exhibiting the periodicity of the symptoms detailed above, together with their vagueness, and the absence of urinary symptoms, fever and leucocytosis, should be suspected of possessing an aberrant renal vessel. Confirmation of the diagnosis is almost wholly dependent on laboratory and mechanical procedures.

Once the condition has been confined to the genito-urinary tract, the chief differential points are *renal* or *ureteral stone*, and *renal neoplasm* —the former because of the colicky nature of the attacks; the latter because of the fact that in retrograde pyelograms the pelvis frequently does not fill. *Stricture of the ureter* and *ureteral kinking* must also be considered. The diagnosis may be made by the x-ray. If on slightly added pressure the obstruction of the vessel is overcome and the renal pelvis is filled, a gap in the ureter may be seen at the point of obstruction. Squaring off of the lower border of the kidney pelvis, because of the sagging of the kidney over a fixed point (the aberrant vessel), is one of the most valuable x-ray signs. Intravenous pyelography is extremely valuable here, in that it serves to confirm the retrograde findings, and also gives valuable information regarding the opposite kidney. In case 1 the diagnosis was made by this means.

Treatment. — Modern treatment falls under three main heads. (1) *Simple division of the vessel.*—If the vessel in question is large there may be a danger of impoverishing the renal blood supply by its ligation. Fitgerald suggests digital compression of the vessel for a few minutes, watching the kidney closely for any change in vascularity. (2) *Plastic operations.*—These include types of operations designed to preserve the aberrant vessel. Among them may be mentioned resection of a portion of the renal pelvis, division, and reimplantation of the ureter. (3) *Nephrectomy.*—This operation is reserved for

those cases in which there is extensive renal damage. Whether or not nephropexy should be done depends on the case. In the two cases reported above it was not necessary. It is our personal view that any kidney, having been once disturbed from its bed and replaced, will do very little moving thereafter because of the formation of adhesions. Engle, Higgins and others believe that simple division and ligation of the vessel are quite sufficient.

SUMMARY

1. Two cases of aberrant renal vessel are reported.

2. Both occurred in males, and both on the left side.

3. Both caused marked symptoms, and in one there was sufficient hæmaturia to suggest a renal neoplasm.

4. Neither case showed nephroptosis, and in neither case was there any marked hydronephrosis.

5. Both were cured by simple ligation and division of the aberrant vessel.

6. The condition of aberrant vessel is briefly described, with particular attention to the symptomatology, diagnosis and treatment.

Case Reports

A DERMOID CYST IN A CHILD

BY A. T. GILLESPIE, M.D.

Fort William, Ont.

O.M., aged 11 years. This girl came under my care on August 10, 1938, complaining of pain in the abdomen. The pain was intermittent, and while examining her she said it felt easier. The abdomen was greatly distended, and a large, firm mass was palpable in the lower part but extended above the umbilicus. In an older person one would consider pregnancy, but as she had had no menses and was only eleven years of age, this was at once ruled out.

She gave a history of becoming larger in the abdomen for almost a year. At times it seemed to be more noticeable than at others. She was very sensitive about it, and refused to put on a bathing suit which her mother had given her. There was no discomfort until three days previous to my being called, when she commenced to have intermittent crampy pains. For the past two months she had had some nausea and often vomited on getting up.

She was removed to hospital, and an enema given, with a rather poor result. Catheterization did not reduce the size of the tumour. X-ray revealed a tumour with a slight opacity towards the right side, and the report suggested a dermoid cyst.

On further palpation the mass was felt to rise out of the pelvis and extend two fingers' breadths above the umbilicus. It was in the mid-line, oval in shape, firm, smooth and slightly movable from side to side; no fetal parts were palpable and there were no fetal heart sounds.

The head and neck were negative. The respiratory movements were normal; no dullness found at the bases of the lung. No crepitations were heard. The heart was not enlarged; no murmurs. The kidneys were negative. The gastro-intestinal tract was negative, except for some constipation.

She was operated on on August 12th through a lower median incision, under ether, and a large bluish mass exposed. Before this could be extricated from the abdomen a pint of dark reddish-coloured fluid had to be aspirated. It was then removed from the abdomen, and found to be twisted (one complete twist on its pedicle, which was attached to the right broad ligament beside the uterus). It was easily clamped, removed and sewed over.

The child made a quick recovery, and convalescence was good except for a slight bronchitis and a small amount of infection in the lower end of the wound.

The pathological report was as follows: "Gross specimen consists of a very large cystic structure measuring up to 13 cm. in diameter. It is found to be made up of several large cystic structures, some of which are filled with a greyish-white grumous material. In others a few fine white hairs can be found scattered about in this grumous material. The walls of the cyst are intensely hæmorrhagic, suggesting a torsion of this cyst about its pedicle. No ovarian tissue could be found in the gross.

"Microscopic report: Sections of the cyst confirm the diagnosis made in the gross. No evidence of malignancy. Diagnosis: Dermoid cyst."

To summarize the main points: (1) one is struck with the youth of the patient; (2) the enormous size of the tumour as compared to her comparatively small abdomen; (3) it was a typical case of torsion of the tumour on its pedicle.

A PREMATURE INFANT WEIGHING LESS THAN ONE POUND AT BIRTH WHO SURVIVED AND DEVELOPED NORMALLY

BY J. S. MONRO

North Sydney, N.S.

The smallest infant to survive, as reported in the medical literature, weighed 600 grams (21.16 ozs.), at birth. I feel, therefore, that a brief report of the male infant which weighed 14 ozs. on the second day and 9¾ pounds at seven months will be of interest. This child was born in a country region, where the facilities for scientific care of a premature infant were completely lacking. In spite of this and, I feel, chiefly due to the interest and care given by the nurse on the case, this tiny infant lived, thrived,

and is now a normal baby of nearly normal weight for its age.

Baby McG. was born about 10.30 p.m., on June 6, 1937, fifteen minutes after my arrival. The child was the third born to the mother, who was twenty-eight years of age at the time. The birth was approximately two months premature. The delivery was normal. The child was alive but so extremely small that I did not expect survival, since there was no incubator available. The nurse bathed the baby in warm olive oil, wrapped it in cotton, and placed it in a basket in a warm oven. No scales were at hand, so the actual birth weight was not obtained, but it was by far the smallest living baby I had ever seen. Shortly after birth the nurse gave the baby two drops of brandy in warm water from an eye dropper. Greatly to my surprise the nurse called me on the telephone the following morning to inform me that the infant was still alive and to request feeding instructions. About 11 a.m., June 7th, the day following birth, the nurse took the baby to a local grocery store, and weighed him on the grocery scales in the presence of the proprietor and another person. The weight of the baby at that time was fourteen ounces, as the accompanying affidavit confirms. For two days the child was given feedings of two drops of brandy and a few drops of corn syrup in warm water from a dropper. On the third day the child was given lactogen, in a dilution of one teaspoonful to one ounce of water, and since that time has been fed lactogen in the full strength dilution (1 part lactogen to 7 parts water), with progressive increases in volume as the baby grew older. For the first ten days of life the child took several droppers of formula each hour. At ten days on the infant was able to suck, and, therefore, was fed from a bottle on a two-hour schedule. During the first two weeks the baby was kept in a warm oven at night.

The weight at 2 months was 3 pounds, at 4 months 6 pounds, at 7 months 9¾ pounds, at which time the body length was 24¼ inches. The child has been generally healthy and normal as to its physical and mental condition. Cereal, vegetable purée, and other usual additions were made to the diet at 6 months.

At present the child is 12 months old, weighs 13 pounds 12 ounces, and measures 25¼ inches.

The accuracy of the reported weight of this infant (14 ozs.) is attested by two affidavits made before Mr. James G. Hackett, N.P., of North Sydney, N.S.—[ED.]

GYNATRESIA

BY L. J. O'BRIEN, F.R.C.S.(C.)

Grande Prairie, Alta.

An unusually attractive, healthy young woman, 22 years of age, consulted me because she wished to marry and had never menstruated. The patient said she had had mild pelvic pain at irregular intervals during the last year.

Examination showed well-developed breasts, pubic hair, feminine in type; labia of average size. There was no trace of an introitus vaginæ. An incision was made where this should be and dissection carried out between the anus and the urethral opening for two and a half inches. No trace of mucosa or vaginal wall was found.

A suprapubic incision was then made. The right ovary was of average size, the left one larger than usual, and both appeared to be functioning. Both tubes appeared normal and each ended in a small body 1.5 cm. long by 1 cm. broad, and 0.5 cm. in thickness. These bodies lay in opposite sides of the pelvis and were plainly halves of a vestigial uterus split in the middle sagitally. The peritoneal covering of the left half was stripped off, but no lead or cavity resembling a vagina was found.

Therapeutics and Pharmacology

THYROID STORM

BY A. R. MUNROE, M.D.

Professor of Surgery, University of Alberta, Edmonton

Although thyroid storm occurs less frequently today than formerly it is still not unknown and it is frequent enough to warrant more than passing attention. Surgeons who were doing thyroid surgery twenty years ago can recall many deaths due to this cause, and are likely to be alert to the onset of the condition, and are in a position to appreciate the vast change that has taken place during that period.

The decrease in the incidence of acute thyroid crisis is due to the careful preparation of patients now universally adopted before any operation on the thyroid gland is undertaken, but this post-operative calamity has not been altogether eliminated. In discussing the management of thyroid storm or post-operative thyroid crisis it is necessary to discuss the details of the preparation for operation.

It is well to remember that: (1) any operation on the thyroid gland, even a simple pole ligation, *may* precipitate an acute thyroid crisis; (2) any toxic goitre without adequate pre-operative preparation *will likely* end in a post-operative crisis; (3) any toxic goitre, even when the patient is carefully prepared for operation by every known aid, *may* terminate in a post-operative crisis.

The measures at our command at present are rest, feeding the patient a high-calorie diet, iodine medication, and administration of glucose. Although it is possible to adopt this treatment outside of hospital it is suggested that the practitioner shift the responsibility for this treatment to the hospital surgeon.

1. *Rest.*—Rest is so important that it is placed first. By rest is *meant* rest, both mentally and bodily. Rest in bed in a quiet room, few or no visitors, and plenty of sleep will alone cause marked improvement in a few days. To secure sleep it may be necessary to administer sedatives, *e.g.*, bromides or one of the barbiturates. After a few days patients who are only moderately toxic may find it restful to sit up in a chair for a short period, say half an hour or one hour morning and evening. Bathroom privileges may be allowed up to the time of operation.

2. *Diet.*—A high-calorie diet should always precede and continue after operation. The diet should consist largely of carbohydrates, as protein and fats increase the patient's metabolic rate. The diet should produce 3,000 to 4,000 calories per day, and most patients are not hard to feed as the appetite is usually abnormally good. Feeding by mouth may be supplemented by intravenous injection of 8 to 10 per cent glucose solution.

3. *Iodine medication.*—Iodine in the form of Lugol's solution is now almost universally given to goitre patients before operation. As it is so easy to give a few drops of iodine three times a day for a month or two to see how the patient acts many patients come to hospital iodine-fast. They have been taking iodine for a period of weeks or months, and have lost one major chance to be put in ideal condition for operation, as they do not again respond to the administration of iodine. If the patient has not been taking iodine it is one of the most valuable aids in controlling hyperthyroidism. It should be stressed that the improvement from iodine is temporary and the patient will receive the maximum benefit from it when administered in 10 minim doses three times a day while in hospital, resting and receiving a high-calorie diet preparatory to a thyroidectomy. Rest plus a high-calorie diet, plus Lugol's solution will result in a marked lowering of the metabolic rate and a marked improvement of toxic symptoms in almost all patients except those who have been taking iodine before coming to hospital.

4. *Glucose intravenously.*—The administration of glucose intravenously in 8 to 10 per cent solution materially aids in controlling the hyperthyroidism and enables the liver to build up a reserve store of glycogen on which the patient can draw after operation.

The length of time necessary to prepare patients for a thyroidectomy varies considerably. Some will require but a few days while others will require 12 to 14 days. When it is felt that the maximum improvement has been obtained thyroidectomy should be proceeded with without delay, otherwise the patient may slip back into a state where toxic symptoms increase again and the reaction to operation will be more severe.

It is well to remember that any operation on the thyroid gland will be followed by a reaction which may vary from a mild disturbance to a severe storm. The mild disturbance will pass off in a few days, and at the end of that time the feeling of well-being is very noticeable. This is the usual sequence to a carefully planned and skilfully performed thyroidectomy. Even today severe reactions are not unknown, and occasionally a toxic crisis or storm may follow simple operations on the gland and its occurrence with fatal termination after a major operation on the gland is likely to occur once in a while in any hospital. It is by far the most frequent cause of death in the thyroid patient and should be eliminated by careful pre-operative management, as once a severe storm sets in most cases terminate fatally.

The symptoms to be watched for are those of thyrotoxicosis multiplied to the nth degree—pulse 200 or uncountable, the patient restless, irritable or delirious. Often there is extreme weakness or collapse from exhaustion, and often coma. The temperature is always high; 106° or more is not unusual. All the aids used to prevent the crisis should be continued after operation, and in the face of a storm treatment should be intensified as death may terminate the case in a few hours. Glucose intravenously should be given continuously. Iodine medication should be pushed and a more rapid reaction obtained by giving it intravenously. It may be given by hypodermic syringe through the tubing used in administering the glucose. Morphine should be given at regular intervals, every four or six hours in quarter grain doses, sufficient to secure rest. Phenobarbitol or other sedatives may be added. Oxygen should be given, preferably by way of the nasal catheter, as this is less disturbing to the patient than the oxygen tent and the amount of oxygen given can be more accurately regulated.

A few cases in acute crisis may be saved by these measures, but the best way to meet any crisis is to anticipate it, and proper pre-operative management will prevent many cases ending up in storm.

DUPUYTREN'S CONTRACTURE.—That in addition to occupational trauma as a determining cause constitutional and hereditary factors play a part in the production of Dupuytren's contracture is shown, according to M. Constantinescu by the reports in the literature of 9 cases (to which a tenth is here added) of its congenital occurrence; and also by its not infrequent familial incidence—in 4 out of 22 cases studied by Krogius and in 12 out of 31 investigated by Schröder. There is also evidence that organic nervous lesions are concerned in certain cases; the contracture has been noted in sufferers from tabes, general paralysis, and syringomyelia, after injury to the brachial plexus or ulnar nerve, in association with lesions of the eighth cervical and first dorsal segments, and in combination with the Horner syndrome. In three of four brothers affected Testi was able to find at necropsy evidence of syringomyelia. Constantinescu's patient, a boy aged 15, in whom the deformity caused little or no inconvenience, had been delivered through a flat contracted pelvis, his genital organs were hypoplastic, but the blood calcium was normal. The deformity was bilateral.—*Zbl. Chir.*, January 22, 1938, p. 191. Abs. in *Brit. M. J.*

Clinical and Laboratory Notes

A DOUBLE SYRINGE FOR THE ADMINISTRATION OF PROTAMINE ZINC AND UNMODIFIED INSULIN*

BY E. M. WATSON, M.D.

London, Ont.

While the insulin requirements of many diabetics may be supplied by single daily injections of protamine zinc insulin, experience has shown that numerous patients require some of the unmodified insulin in addition to the protamine zinc variety for the adequate control of their disease, especially during its more acute phases. The protamine zinc insulin, on account of its slow mobilization in the blood stream, is often not readily available for the immediate metabolism of the carbohydrate introduced with the meals, consequently rather marked rises of the blood sugar are apt to occur. This postprandial hyperglycæmia and accompanying glycosuria is especially prone to develop after breakfast. An attempt to avoid its occurrence by increasing the dose of protamine zinc insulin may result in more or less severe hypoglycæmic reactions. A modification of the diet in a way that the carbohydrate value of the breakfast is reduced and that of the other meals increased accordingly may be effective in certain instances. A plan involving multiple meals is a bothersome procedure in any case.

The most satisfactory method is by some combination of protamine zinc insulin and unmodified insulin whereby the latter takes care of the immediate requirements until the former begins to act. Lawrence and Archer[1] recommend that the two insulins be mixed in a syringe and given as one injection, claiming that the individual qualities of the two types of insulin are maintained under such conditions. While this combination appears to serve the desired purpose in some cases, a study of the daily fluctuations of the blood sugar in a number of our patients indicates that the effect of the combined dosage is little if any different from that resulting when the sum of the two doses, considered in terms of units, is administered in the form of protamine zinc insulin alone. Apparently most of the unmodified insulin when brought in contact with the protamine compound is converted into protamine insulin and behaves as such. Campbell, Fletcher and Kerr[2] mention their success in giving protamine and unmodified insulin as a single injection with a long, narrow-bore syringe and care in avoiding mixing of the fluids.

In order to obtain the maximum satisfaction, it is preferable to administer the two kinds of insulin separately. The objection to this practice is, of course, the multiplicity of injections. In an attempt to circumvent this disadvantage and at the same time avoiding the admixture of the two liquids, the double-barrelled syringe described below was devised.

DESCRIPTION OF THE DOUBLE SYRINGE

The instrument consists of two 2 c.c. glass syringes connected to a three-way metal stop-cock. By adjusting the stop-cock the syringes may be emptied independently of one another. Fig. 1 shows the various parts assembled as for use. The syringes have been fixed in position by means of an adjustable clamp attached to a frame which has been fashioned from 16 gauge brass plate. Manipulation of the instrument is facilitated by a thumb-rest which is also fitted to the frame. Fig. 2 shows the component parts

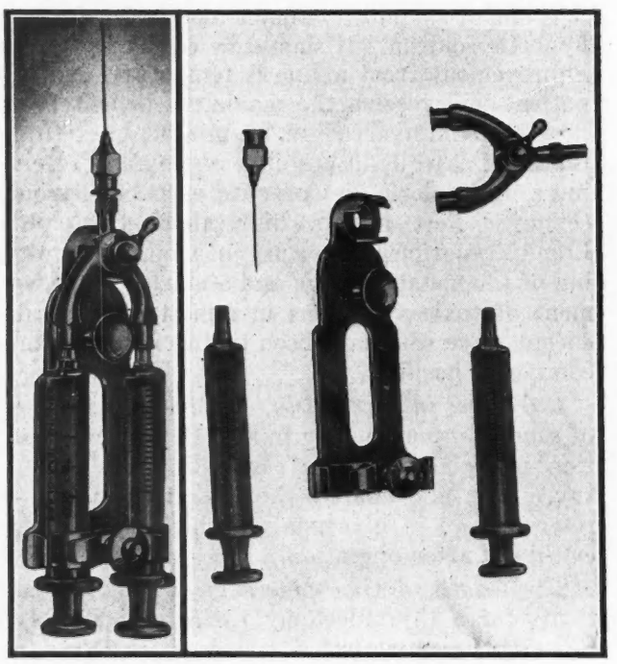

Fig. 1 Fig. 2

disassembled as for sterilization. The stop-cock unit which is shown resting loosely in the turreted receptacle of the frame in Fig. 1 has been removed. All the metal parts are chromium-plated.

In use, a somewhat longer needle than is usual for injecting insulin is employed. The proper amount of unmodified insulin is drawn into one syringe and the dose of protamine zinc insulin into the other. After inserting the needle rather deeply, the unmodified insulin is deposited in the subcutaneous tissues. The needle is then withdrawn slightly, re-inserted in a different direction and the protamine zinc insulin injected. A nurse may complete the treatment of several patients with the device in a short time by merely changing the needles between the individual operations.

* From the Department of Pathological Chemistry, University of Western Ontario Medical School and the Metabolism Service, Victoria Hospital, London, Ont.

So far, this type of syringe has been employed only within the hospital but it has proved to be an acceptable innovation both to the patients and to the nursing staff. Further, all-day blood sugar curves have demonstrated that the effects of giving the two insulins by means of the double syringe are comparable with those resulting from the injection of the individual doses in widely separated parts of the body.

SUMMARY

On account of the delayed action of protamine zinc insulin, many diabetics require the supplemental advantage of the rapidly acting unmodified insulin for the adequate control of their diabetes. A double-barrelled syringe for the injection of the two types of insulin, without their admixture, is described.

The apparatus described in this paper was constructed by Mr. Arthur Barber, technical assistant in the Department of Pathological Chemistry, University of Western Ontario Medical School.

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Editorials

FADS AND FALLACIES IN DIET

THERE is great satisfaction in collecting the fads of our profession. At any rate, it is frequently done. Dr Russell M. Wilder,* of the Mayo Clinic, has recently permitted himself to reflect on some of the fads and fallacies that have arisen with regard to our food. It is true, he says, that we have laid down a highway paved with known facts regarding vitamins: Eykmann, Takaki, Gowland Hopkins, Funk, these and many others have done the paving and have done it well. But, says Dr. Wilder, we have yet to convince people that this road is safe for travel and to get them to follow it. The opportunities are many for the exploitation of its travellers and for the development of fads. So much is this so that many otherwise well informed people, including physicians, have failed to realize the well established aspects of nutrition in their distrust of the many obvious exaggerations regarding it. More than that, there have been tendencies to over-conservatism on the part of some recognized authorities, who are inclined to advise people merely to follow ordinary mixed diets. This is only an instance of extreme caution which is gradually being modified.

Far more difficult to deal with are the attempts to exploit the newer knowledge of nutrition. Dr. Wilder's address is concerned chiefly with what is being done to combat this by the Council of Foods of the American Medical Association. The whole function of this body is so to judge food products and their advertising that the resultant mass education will be along accurate lines. Manufacturers of food products and those interested in the promotion of natural or processed foods for which claims are made in relation to the promotion of health are asked to present to the Council both the material itself and the advertising about it. If accepted by the Council (and only then) the advertising is allowed in publications of the American Medical Association and the Council's "Seal of Acceptance" may be displayed in connection with the food.

The work of the Council has increased enormously. It is gratifying to learn that there is widespread, though unfortunately not general, cooperation on the part of the commercial elements. The wise recognize the value of truthful advertising, and the prestige of the Council puts them completely above any suggestion of unfairness or self-seeking.

Nor does the Council limit itself to criticism. It will combat prejudice which may arise either from faddists or the effects of uncontrolled advertising. Such wholesome foods as oleomargarine and white bread, *e.g.*, have suffered much from prejudice, and the Council has made it its business to set out the true facts regarding them. Incidentally, the Council justly condemns the term "healthful" in the advertising of foods. It has a false implication. "Wholesome" is not only a more sensible word, but it makes no false claims: it has the ring of true coin.

* *Sigma Xi Quarterly*, 1938, **26**: 73.

But the Council has a hard task. It tries to teach people to follow plain and well-established facts about food. But there is very little exciting and nothing novel enough in the principles of good nutrition, and too many people want too much novelty. For those who are looking for wise guidance, however, its work shines as a beacon on the road mentioned by Dr. Wilder.

H.E.M.

THE DIFFERENTIATION OF "FEBRILE CATARRH" AND "VIRUS INFLUENZA"

IN 1933 Smith, Andrewes and Laidlaw[1] were able with bacteria-free naso-pharyngeal washings of influenza patients to produce in ferrets after intra-nasal instillation a characteristic catarrhal and febrile reaction. This disease was transmissible in series from ferret to ferret, and those that recovered were immune to further inoculations. In the following year the work was confirmed by Francis[2] in the United States, and since then virus has been isolated from other sources in England and also from Russia, Germany, Hungary, the West Indies, etc. Virus has also been isolated from swine influenza and it is now known that not all human viruses are serologically alike. One is almost overwhelmed with the variety of immunological data that have accumulated in the comparatively short period that has elapsed. For instance, a survey has been made of the presence of antibodies in selected populations, *i.e.*, in those never exposed to influenza (the inhabitants of the island of St. Helena) as opposed to peoples of countries where the 1918 epidemic was known to strike. There has even been a human experiment on the value of vaccination against influenza. One of the workers at the Medical Research Council's laboratory in Hampstead was accidentally infected by a coughing ferret and developed typical influenza with the formation of specific antibodies not previously present in his serum, an observation that makes it reasonably certain that the virus from the ferret is the cause of human influenza.

It has probably been surmised that one of the difficulties that had to be surmounted in an enquiry into the causal agent of influenza was the clinical differentiation of bona fide influenza from other febrile upper respiratory conditions. Actually this was the case, and the failure to isolate virus from one local epidemic symptomatically resembling another outbreak from which virus could be isolated necessitated the employment of a clinician to collaborate with the laboratory investigators. This enabled the clinician to separate the epidemics into those from which virus could be isolated, the symptoms of which were classed as influenza, and these could be contrasted with outbreaks in which no virus was isolated and which have been tentatively called "febrile catarrhs". It is our primary purpose here to summarize the main findings that have been elicited by this clinical collaboration of Dr. Stuart-Harris with Drs. Andrewes and Wilson Smith, and which have been published as a special report by the Medical Research Council this year.[3]

Four outbreaks resembling influenza were studied in 1936, and from none of these was virus isolated. They occurred respectively at the barracks in Woolwich in February, at the R.A.F. depot in Eastchurch in May, at a naval barracks near Chatham, and at Rugby school in November. Detailed notes were made on over 50 of these several hundred cases. Similar detailed clinical notes on true virus influenza were obtained on over 100 patients seen during the influenza epidemic of December, 1936, to February, 1937. Considerable uniformity occurred in the clinical picture in the influenza group, allowing for differences in severity. In the majority these symptoms enabled a differential diagnosis from "febrile catarrh" to be made. Briefly, in influenza the onset is

1. SMITH, W., ANDREWES, C. H. AND LAIDLAW, P. P.: A virus obtained from influenza patients, *The Lancet*, 1933, **2**: 66.
2. FRANCIS, T., JR.: Transmission of influenza by filterable virus, *Science*, 1934, **80**: 457.
3. STUART-HARRIS, C. H., ANDREWES, C. H. AND SMITH, W., WITH CHALMERS, D. K. M., COWAN, E. G. H. AND HUGHES, D. L.: A study of Epidemic Influenza; with Special Reference to the 1936-37 Epidemic", Medical Research Council, Special Report Series, No. 228, 1938.

sudden, constitutional symptoms predominate, the cough is short and dry, the voice husky, and there is posterior pharyngitis with no exudate. In the febrile catarrhs the onset is insidious, local respiratory symptoms predominate, cough is paroxysmal and productive, the voice is hoarse, tonsillitis occurs along with pharyngitis, and exudate is present. Below is the authors' table summarizing the main points of difference in the two diseases.

DIFFERENTIAL DIAGNOSIS OF EPIDEMIC INFLUENZA AND FEBRILE CATARRH

	Epidemic influenza	*Febrile catarrh*
Onset	Sudden.	Insidious.
Symptoms	Constitutional predominate.	Respiratory predominate.
Cough	Short and dry.	Paroxysmal, irritating, painful, productive.
Voice	Husky.	Hoarse.
Throat	Posterior pharyngitis; no exudate.	Tonsillitis and pharyngitis; exudate common.
Fever	Sometimes diphasic.	Rarely diphasic.
Complications	Bronchiolitis and pneumonia.	Bronchitis and broncho-pneumonia.
Epidemic	Short, with rapid peaking.	Prolonged and grumbling.
Contacts	Clinical picture uniform though graded in severity.	Clinical picture variable; tonsillitis in contacts.
Leucocyte count	Not diagnostic.	Not diagnostic.
Virus	Influenza virus recoverable from pharynx.	Influenza virus not concerned.

The interest centres on the fact that for the first time one may be reasonably sure that the particular outbreaks reported above are significantly different in etiology, one being primarily a virus disease and the other not. Any physician who suffered from epidemic influenza and has also had febrile upper respiratory attacks will agree that there is a difference, and will not be surprised that the two entities have been separated by laboratory methods.

Other conditions that may cause confusion in diagnosis are streptococcal tonsillitis, pneumococcus (lobar) pneumonia, gastroenteritis, and nervous disorders. In the first the pain in the throat is more severe, and there is cervical node enlargement with tenderness. Only rarely are the constitutional symptoms of lobar pneumonia so in advance of the localizing symptoms and signs as to cause difficulty in diagnosis. A word should be said of gastroenteritis, since the diagnosis of "gastric 'flu" is frequently made. In the experience of the present reporters gastric symptoms may be present at the onset of epidemic influenza, but with continued diarrhœa and vomiting abdominal disease should be suspected. Only two cases with gastric symptoms were tested for virus. One, which later developed typical symptoms of influenza, yielded virus, while the other, with symptoms wholly gastro-intestinal, did not. In other words there is as yet no proof for the diagnosis of "gastric 'flu" in the absence of respiratory symptoms. Mental drowsiness in influenza is only rarely so severe as to cause encephalitis to be suspected.

Tribute is due to the original discoverers of the virus, as it has greatly stimulated work on influenza. Since the mouse may now be used to transfer virus progress is likely to be rapid, and vaccination of human beings will undoubtedly soon be re-attempted in light of the recent observation that not all strains of virus are identical.

ARNOLD BRANCH

LIVER THERAPY IN HYPEREMESIS GRAVIDARUM.—E. Mühle describes a case of hyperemesis gravidarum in the second month of the pregnancy in which he injected liver extract to counteract a severe anæmia. All the usual therapeutic methods had failed to give relief, but this was obtained after the first injection. In the past year he has treated in this way twenty cases, of which ten were severe, with only one failure. Only two patients required hospitalization. In all cases a diet poor in proteins and fats and rich in carbohydrates but with no milk was prescribed. Rest in bed was advised where practicable, but not enforced. Intramuscular injections of liver extract were administered daily in severe cases, on alternate days in mild ones, until all the symptoms had disappeared. The author does not know of any contraindications to this treatment. There is no explanation of this favourable action of liver extract. The doses are too small to account for its rapid action, which is in a sense similar to that of liver in the treatment of bismuth and lead poisoning.—*Zbl. Gynäk.*, March 19, 1938, p. 645. Abs. in *Brit. M. J.*

Editorial Comments

The Cancer Campaign

The New Section in the Journal

Readers of the *Journal* will have noticed that a new Section has been started in the *Journal*. It is called "The Cancer Campaign" and is the *Journal's* contribution towards Canada's attempt to control this dread affliction more fully. It is intended that the Section will appear monthly, at least so long as it is necessary. It will contain reports of the doings of the new Canadian Society for the Control of Cancer, which has now got away to a good start, of the deliberations of the Association's Committee on Cancer Control and the Cancer Study Committee. It will endeavour to keep our readers posted as to important developments in the matter of cancer throughout the world, in all its phases. Interesting items of news relating to cancer will be found here, as well as short abstracts of articles in other journals. A selected bibliography on the subject of cancer will appear each month. No attempt will be made to make this bibliography complete; this would be futile in view of the immense literature which is being put out. Only those articles which in the judgment of the Editor are informative to us here in Canada and will be of use to those who are actively engaged in the campaign will be listed. The differential diagnosis of cancer, the best forms of treatment, statistical information, the public health side of the cancer problem, and the education of the laity will all receive attention. We shall also be pleased to hear from our readers on any topic relevant to cancer, and will stand ready to publish any such communications which appear to us to have practical value. We hope to make the new Section a sort of clearing-house for Canada in the matter of cancer. Lengthy presentations on cancer will, however, appear elsewhere in the *Journal*, that is, in the usual place for contributed articles. In course of time a considerable amount of factual material on the subject of cancer will have been conveniently concentrated in a small space which should be of value to all. A.G.N.

The Osler Scholarships

One of the many good works of the Canadian Medical Association, one the value of which can hardly be calculated, was the establishment in 1929 of two Scholarships in memory of Sir William Osler. Nominations to the incumbency of these are in the hands of McGill University and of the Montreal General Hospital. The holders are enabled to spend time at some large clinical centre or centres. One of those appointed in 1936 was Dr. Stuart R. Townsend, of Montreal, who sends us an account of his stewardship.

In August, 1936, Dr. Townsend proceeded to Boston as Research Fellow in Medicine at Harvard Medical School and Clinical Assistant at the Peter Bent Brigham Hospital. Here he spent a year working on the subjects of hypertension and nephritis, as well as attending lectures and clinics. During this time three articles were written and published. These are "Studies on the anæmia of chronic glomerulonephritis and its relationship to gastric acidity" (with Edward Massie and Richard H. Lyons), *Am. J. M. Sc.*, 1937, **194**: 636; "Hyperindicanæmia in renal insufficiency and the significance of the diazo reaction", *J. Lab. & Clin. Med.*, 1938, **23**: 809; "The action of urea, indican and phenol on red cell hæmolysis (with M. Pijoan) *Proc. Soc. Exper. Biol. & Med.*, 1937, **37**: 236.

Then he went to Baltimore, where he became Assistant in Medicine at Johns Hopkins and Assistant Resident in Medicine at the Baltimore City Hospital. Some original work was done with Drs. Warde Allan and William Carnes here also. Four other papers on clinical subjects are in preparation, two of which are ready for publication.

Dr. Townsend expresses himself in a letter to the General Secretary as proud and very grateful for the opportunities which the Scholarship has afforded him. He has returned to Montreal to practise and has obtained an appointment at the Montreal General Hospital.

The Association is interested in Dr. Townsend's account of his work and wishes him all success. We commend him for sending us his report, an action which, it is desirable, should be copied by future holders of the Osler Scholarships. A.G.N.

A New Plan for Biological Abstracts

Many readers of the *Canadian Medical Association Journal* will be interested in the new plan for the publication of *Biological Abstracts* in 1939. *Biological Abstracts* first appeared in 1927 and for ten years was assisted financially by a number of grants, chiefly from the Rockefeller Foundation. It is now the desire of the Board of Trustees of *Biological Abstracts* that it become self-supporting. The new plan for 1939 was devised with this end in view. The plan may be divided into two parts, (*a*) a maximum coverage in abstract form of current and recent literature in the various fields of biology and the biological sciences, and (*b*) the issuance of *Biological Abstracts* in sections, as well as in a complete whole. The latter plan enables those interested to purchase at a reasonable cost that section in which they may be particularly interested.

Readers of the *Canadian Medical Association Journal* will be interested mostly in Section II,

"Abstracts of Experimental Animal Biology", which includes abstracts of papers appearing in the fields of physiology, nutrition, pharmacology, pathology, anatomy, embryology and animal production. This will be the largest Section of the *Abstracts* and will be available to subscribers for 1939 at the price of $9. Abstracts of papers of general and special interest in the *Canadian Medical Association Journal,* which have regularly appeared in *Biological Abstracts,* will largely, if not entirely, be contained in Section II. There will also be interest in Section III, "Abstracts of Microbiology and Parasitology", including immunology, bacteriology, viruses, parasitology, protozoology and helminthology, at $5 for 1939. Section IV, "Abstracts of Plant Sciences", includes pharmacognosy and pharmaceutical botany amongst the other botanical sciences. Section I is concerned with general biology and Section V with the zoological sciences. Subscribers to any one Section will receive the complete index to the entire five sections. Further information may be obtained from the Business Manager, Biological Abstracts, University of Pennsylvania, Philadelphia, Pennsylvania.

ELDON M. BOYD

Corrigendum

Dr. J. P. Boley, of Windsor, Ont., desires to call attention to certain errors in statement which appeared in his paper entitled "Squint" (*Canad. M. Ass. J.*, 1938, **39**: 560). On page 562, second paragraph, line 12, read "The extra accommodation brings on an added and often undesired *convergence*". In the same paragraph line 20, read "This may be followed by a deficiency in *divergence* power".

Special Article

DIET AND NUTRITION

IODINE IN NORMAL NUTRITION*

BY WALTER R. CAMPBELL, M.D., F.R.S.C.

Toronto

XI.

Physicians are now accustomed to expect profound physiological effects from infinitely small amounts of substance. One of the first of such substances to be studied was iodine, the discovery of which was perhaps the most useful by-product of the Napoleonic wars. The British blockade of the French coast cut off the supplies of Chilian saltpetre required for the manufacture of gunpowder. Decomposing calcium nitrate with the ashes of kelp as a source of potash, Courtois in 1811 found iodine in the vats. Within the next ten years the sources and principal properties of this new element were described, and Coindet correlated the iodine content of the ashes of sponges and seaweeds with the knowledge existent since ancient times of their favourable influence on goitre. He used the element in the treatment of such cases with happy results in some but with unfavourable results in others. These untoward toxic manifestations prompted him to issue a warning that iodine should only be used in limited doses and under careful medical supervision, a warning which has been insistently repeated and consistently ignored in the last one and a quarter centuries.

Iodine is widely but sparsely distributed in nature; indeed the amount is frequently recorded in parts per billion. Only in the sodium nitrate beds of Chile and Bolivia does it reach a concentration of 0.2 per cent.* There are few minerals in which it is an essential component. All rock contains some iodine, but the element is most abundant in those sedimentary types which contain fossils. In most rock formations the iodine is supposed to be dissolved in the connate water and only gradually leached out. Disintegration of the rock by weathering gives rise to soils of various types. Those of a sandy character retain but little iodine, while the more colloidal types, such as the clays, usually adsorb part of the iodine leached out of the rock. In mountainous regions and recently glaciated areas iodine is scarcer than in other regions, particularly those which have been below sea level. For this reason a considerable part of Canada is low in iodine. While this is particularly well known, from the results on animals and man in the Great Lakes basin and in the mountainous regions of the West, there is little reason to doubt that a similar situation exists in our more northerly regions.

* From the Department of Medicine, University of Toronto, and the Medical Service, Toronto General Hospital.

This is the eleventh in the series of articles on Diet and Nutrition, prepared under the auspices of the Association's Committee on Nutrition. The previous articles can be found in the *Journal*, 1938, **38**: 277, 387, 491, 586; **39**: 76, 179, 280, 389, 483, 578.

* For the purposes of this article it has not appeared necessary to quote many exact figures. For these the reader is referred to the literature, excellent summaries being McClendon: Physiological Reviews, 1927, **7**; and Orr and Leitch: Special Report No. 123, Medical Research Council, 1929. Though many of the older figures have been confirmed repeatedly the methods available were not so satisfactory as those of today, and even at the present time relative order of magnitude is probably more truly representative of the facts than some of the actual figures recorded.

Iodine has a great affinity for organic matter, and plants grown in a particular soil contain more iodine than the soil itself but vary greatly in iodine content from the same species grown elsewhere. Coal and oil likewise contain considerable iodine, probably because of their derivation from living matter. While it is being continually swept toward the sea by rivers and streams the aquatic plants take up a considerable amount of it. The concentration in the sea water itself is not very great, most of the iodine uniting with organic matter. Thus the ash of kelps and other sea plants is high in iodine content while sea fish contain ten to a hundred times as much iodine as fresh water fishes. Salt beds from ancient dried-up seas contain iodine but this is largely lost in the modern processes of purification of the salt.

Since but little iodine is carried landward in water vapour regions more than three miles from the sea benefit but little from the iodine content of the rainfall. As fuels have a relatively large iodine content it is probable that some of it, though largely concentrated in the soot, is discharged into the air of manufacturing communities. It is known that the air of cities contains more iodine than that of non-urban regions, but it has been shown that all of this iodine is removed by filtration of the air so it probably exists combined in organic form.

Small amounts of iodine are present in all foods, the quantity in animal tissues other than sea foods and thyroid being less than that of normal blood—13 γ per 100 c.c. (1 γ = 0.001 mg.) or 130 parts per billion. The variation is much less than in plant foods whose various species contain differing amounts of iodine even though grown on the same land. The iodine content of milk is small, but may be ten to one hundred times as great in non-goitre areas as in those in which goitre is prevalent. It undergoes seasonal variations probably related to the iodine content of the food being consumed. The thyroid gland contains iodine, as was shown by Baumann, in the highest percentage of all animal tissues. There is some seasonal variation and some evidence that the amount is greater in females than in males. It is also probable that like the blood it varies with the changes in the sexual cycle. It may be much enriched by administering small doses of potassium iodide.

In surveying the effect of iodine in small doses on mammalian metabolism it would seem probable that its effects are largely exerted through its conversion into thyroxin by the thyroid gland. In cases where such conversion does not take place, for example, in the cretin, the effects are absent, while the administration of preparations containing thyroxin exerts the characteristic effect. Thyroxin is a catalyst catalysing all the physiological functions. It is essential for a complete differentiation of the brain and for proper growth of the individual. Overdosage of thyroxin may give rise to characteristic symptoms some of which are not identical with those of iodine overdosage. In the writer's opinion there is little to recommend the view that abnormal thyroxins are a feature of thyroid disease.

The adult human body, Kendall estimates, contains about 20 mg. of iodine, an amount which, from McClendon and Hathaway's data, could be absorbed from the food available in the region in about five years. Perhaps half of this iodine is quite inactive, being in storage in the thyroid. One-third of the remainder is probably present in inorganic form, and, roughly speaking, 10 mg. of thyroxin might be contained in the organic fraction. As Boothby has shown, such an amount is sufficient to raise the metabolism of a myxœdematous individual 28 per cent, or, in other words, approximately to the normal level. It deteriorates at the rate of 10 per cent per day. Some apology may be necessary for these rough calculations as well as for the deduction that the normal thyroid reserve of organic iodine compounds is ten times the daily requirement. But this means a release of 600 γ of iodine per day, whereas from the slender data available some 15 γ is the minimum intake for adult iodine equilibrium. The "internal circulation" of iodine or the iodine reclaimed from degraded thyroxin must then represent a very considerable part of the metabolic iodine exchange, and emphasizes the necessity for long-period experiments on iodine metabolism.

In view of the many factors entering into the matter the minimal requirement for any substance is by no means the most suitable amount to provide. At least three times this amount is desirable and since it has been shown that the minimal amount required by children is three times that of the adult one must allow 50 to 150 γ per day as the suitable intake of iodine. In many different regions of the world the impossibility of ingesting sufficient iodine in the foodstuffs available is apparent from the analyses which have been done. This is particularly true of the larger figure which affects children but will likewise be true in adults during the so-called physiological epochs, puberty, the menstrual cycle, pregnancy, lactation, as well as during infection, when an increased requirement for iodine exists. Where such a deficiency exists goitre is prevalent particularly at the pubertal period. This is true not only of simple goitre but of the toxic type as well.

The empirical use of substances now known to contain iodine for the cure of thyroid disease goes back at least thirty-five centuries. Thyroid gland, ashes of sponges, or seaweed, and certain mineral spring waters, etc., were known to be valuable. With the isolation of the element itself 127 years ago a great deal of experimental work proved its influence both for good and, in excessive doses, for bad. Though somewhat diminished by the alarming results of overdos-

age and later overshadowed by the growth of the germ theory of disease its therapeutic use has never wholly died out and in the last quarter century has been revived.

Stimulated by the experiments of Marine and others, a very complete control of the goitre problem has been attained in Switzerland, and much has been done in other countries. While precipitating influences play their part, a fundamental rôle in thyroid disease must be assigned to iodine deficiency and it is apparent that only prolonged deficiency is of practical importance. Satisfactory surveys either of the clinical or the chemical problem in Canada have not been made, but sufficient is known by analogy to justify a nation-wide attack on these problems now being dealt with only in desultory fashion. Due to the distribution of population it is already clear that the great majority of our people are subject to relative iodine deficiency, and it is well known that its effects on the mental and physical state of the inhabitants will become more pronounced in succeeding generations. Various plans have been advocated for provision of the necessary iodine. The use of a fertilizer containing iodine will improve the yield of many crops and the health of man and animals subsisting on that soil, but such a project seems somewhat impractical. Iodization of water supplies has been tried with benefit in certain cities, but neglects the non-urban population. Administration of iodine as a drug is effective but does not reach the whole population, nor is it likely to be used continuously.

It is known that iodine in small doses over long periods of time is more effective than large doses at intervals and lacks the danger of the toxic effects of the larger dose. The most effective solution at present seems to be the addition of small amounts of iodine to salt. This has been done and is now available to families alert to its advantages but fails to reach a great part of our population. To ensure its benefits compulsory iodization of all salt sold for human consumption will be necessary. Where this has been done, as in Switzerland and Austria, the results have been most gratifying.

Some question has arisen whether or not the amount of iodine used in iodozing the salt on this continent, which is ten times the amount used in Switzerland, may not be productive of toxic symptoms, or even initiate definite hyperthyroidism. While it is unfortunately only too frequently that one encounters dangerous or even fatal effects which have been produced by iodine overdosage I have never encountered a case arising from the use of iodized salt alone. It is surely incumbent on anyone publishing such a case to supply more than *post hoc* evidence. When idiosyncrasy to iodine is excluded and the possible use of a patent medicine, be it goitre cure, cough cure, corn cure, white ointment, or tonic mixture is reluctantly acknowledged, the remaining cases to be ascribed to iodized salt will become extremely few in number. Were compulsory iodization of all salt in force a smaller proportion of iodine would almost certainly be adequate, but the monetary saving would be negligible. The larger quantity of iodine seems more desirable under present circumstances where it may be somewhat irregularly used as table salt.

In default of a national program it must fall on every physician to advocate the widest possible use of a suitable preparation of iodine by the public. It should not be forgotten that the situation calls for prevention of iodine deficiency rather than cure of its long-continued effects, and that prevention for the young begins with adequate iodine intake by the pregnant woman. One of the most valuable uses to which a pre-natal clinic could be put would be the training of the expectant mother to use sufficient iodine both for her own good health and for that of the child. If iodized salt were not used one-fourth to one-half a grain of sodium iodide weekly during pregnancy and the lactating period would prevent congenital goitre and start the infant with enough of this essential food. Such a dose, however, would exceed by many times the adult requirement even at the other physiological epochs, and continuous use of iodized salt at the table (not in the cooking) may be recommended instead.

NOISE AND ITS EFFECT ON HUMAN BEINGS: NOISE-CONTROL AS A BY-PRODUCT OF AIR-CONDITIONING.—In their dissertation on noise and its effect on human beings G. P. McCord, E. E. Teal and W. N. Witheridge conclude by saying that the American Medical Association's Committee on Air-Conditioning recognizes that proper air-conditioning is one factor tending to diminish the ill effects of noise of some types. The procurement of closed windows, doors and other sound barriers commonly associated with artificial climates in public buildings, office buildings, department stores, theatres and so on may eliminate as much as 75 per cent of the noises of extraneous origin. In industry air-conditioning offers little promise of protection against noise for workers employed near the origin of the noise. Vibration in ranges below audibility has a prominent rôle in the production of injuries arbitrarily classed as "noise-diseases". Although inaudible vibrations may involve occupied areas that may be air-conditioned, obviously no protection can be secured from such vibrations by air-conditioning. The compilation of material making up this report presents extensive evidence that genuine injury is widespread as a result of noise-action and that noise-deafness is the chief of these dysfunctions in terms of both frequency and severity.—*J. Am. M. Ass.*, 1938, **110**.

Men and Books

THE MEDICAL LANGUAGE OF ST. LUKE*

BY H. E. MACDERMOT

Montreal

In addressing you this morning I am taking part, with my colleagues,† in one of those observances by which the association between medicine and religion is kept fresh and strong. I need not now say how close that association is. It will be enough to remind you that in ancient times the priest and the physician were one. The complex developments of medicine nowadays may seem to set the two sharply apart, but there has been no real divergence. Indeed, the aims of medicine in some respects still are so intimately blended with those of religion as to be indistinguishable.

For example, I suppose it may be said that one of the functions of religion is the bringing of peace to the mind. Is that any less the aim of the physician? Let me quote from the apparently arid pages of a medical treatise to show what I mean. The extract is from a textbook on medicine by the late Sir William Osler; he is speaking of the relief that may be given by the physician to the anguish of the confused, distressed and weakened mind; he says;

> "In all ages, and in all lands, the prayer of faith, to use the words of St. James, has healed the sick; and we must remember that amid the Æsculapian cult, the most elaborate and beautiful system of faith healing the world has seen, scientific medicine took its rise. As a profession, consciously or unconsciously, more often the latter, *faith* has been one of our most valuable assets, and Galen has expressed a great truth when he said, 'He cures most successfully in whom the people have the greatest confidence.' "

I may add that not many textbooks so finely distil this spirit of the healing art, but then we have had only one Osler.

Our Church has wisely and beautifully perpetuated that association in this Medical Sunday following St. Luke's Day. For the occasion it has seemed proper to me to say something about St. Luke from the point of view of a physician.

As is not unusual, the deep interest with which we regard St. Luke is partly because we know so little about him, and even of that little much is gathered by inference. It is not for me to do more than assimilate something of what has been brought together by the numberless minds which have dwelt on St. Luke's writings with such intensity as to evoke a very definite personality.

I will adopt the generally, if not universally, accepted view that St. Luke was a physician, and that he wrote both the Gospel which bears his name, and the Acts of the Apostles; a single work in two parts, really. Nothing is known about his life before he appears as a companion of St. Paul at Troas, and even after that the direct records of him are extremely scanty. He was probably born in Antioch. The evidence for that, so far as I can gather, is strong, but not conclusive. That he was a Gentile, and well educated, is known for certain, and there is much to suggest that he was a Greek. But there is something also to be said for the view that he was a Roman.

We do not even know by whom he was converted to Christianity, or when. It is a pleasant surmise that he acted as St. Paul's physician, and that it was the Apostle's magnetism which was responsible for the conversion. All we can be sure of is that St. Paul was fighting ill-health for much of his life, and that Luke was his companion for part of this time. We would expect that a personality as strong as that of St. Paul would deeply influence a mind as keen as that of St. Luke, but we must leave it at that.

How do we know that he was a physician? There are the statements of St. Paul, which are quite definite, but I think it is more interesting to let St. Luke reveal himself unconsciously in this respect through his writings. Fortunately, a man is bound to express himself in what he writes, and even if the view thus gained is oblique, it still may be quite distinct.

If his were the only Gospel our investigation into his medical qualifications might not be so fruitful, although one might suspect him even then. But the suspicion strengthens almost to certainty when we compare the different Gospels, especially when we realize that Luke drew much of his material from the others, especially from St. Mark. If he had written independently we would not have had those modifications of the other accounts which indicate the medical writer.

It is true of course that he had other sources. He too used the so-called "Q" records, (German *Quelle*), and he also did his own questioning of eye-witnesses and gathered his own material. This he tells us himself in the preface to his Gospel. We can but send a sigh after any notes that he made, but we have none of the original manuscripts of the New Testament writings, and it is hardly possible that any exist.

For the literary aspect of his Gospel I have little to say, except to recall the obvious difference between the texture of his writing and that in the other Gospels, the careful, orderly arrange-

*An address given at the Morning Service in Saint George's Church, Montreal, on October 23rd, in commemoration of St. Luke's Day.

†The lessons for the day were read by Drs. George Brown and W. W. Francis.

ment of the narrative, the indefinable quality in the expression of the educated, observant mind. If we knew nothing about their authors could we tell which of the Gospels was written by a Greek convert rather than by one of Christ's disciples? Perhaps not. But no one could hesitate in ascribing to the writer of St. Luke's Gospel a degree of culture and a literary power far above that of the others. Let it be quite clearly understood that I am concerned now only with the one small point regarding the medical aspects of Luke's writing. As Professor Burkitt says in his *Gospel History and Its Transmission:* "Morally, ethically, spiritually, these (first) three Gospels are all on the same plane."

Wherein, then, does Luke betray his medical training? First of all, as regards the miracles of healing, and to some extent the others as well, his accounts are more circumstantial than those of the other Evangelists: secondly, he must have been well acquainted with the diseases he described; thirdly, he used language which scarcely anyone but a medical man would employ, exhibiting a knowledge of the technical medical terms found in the extant medical writers, such men, for example, as Hippocrates, Dioscorides, Aretæus, Galen, etc. It is quite true that the educated Greek layman of those times was apt to introduce medical terms into his ordinary discourse. But, on the other hand, it is well recognized that Greek *medical* writers were wont to use words to which they were accustomed in their profession, even when dealing with unprofessional subjects.

It is not difficult to show that Luke's medical terms were those of the Greek medical literature of the time, since, as Dr. Hobart states in his *Medical Language of St. Luke* (and he is my chief guide in this matter), the Greek medical phraseology was of an unusually conservative nature, the same class of words being used in it from the time of Hippocrates to that of Galen (nearly 600 years). Another point is that a trained physician will very likely show tendencies of his training in such matters as closeness of observation, and in his *preference* for stories of healing, which is precisely the case with St. Luke. Some examples of these characteristics may now be given.

At the very outset it may be remarked that St. Luke alone records Our Lord's saying, "Ye will surely say unto me this proverb, Physician heal thyself." The proverb was well known, but apparently Our Lord's use of it made a greater impression on St. Luke than it did on the others.

In the healing of Simon's wife's mother, St. Luke gives details not mentioned by St. Mark and St. Matthew. He speaks of the fever being "great", and adds "he stood over her and rebuked the fever." Now, the designation of the fever as "great" is entirely in keeping with the medical teaching of the day, which separated fevers into "great" and "small". The "standing over her" gives us the picture of our Lord watching the woman before doing anything. It is a detail which would catch the physician's eye, just as the note that "He rebuked the fever" shows interest in the method of cure. A similar addition is found in the instance of healing "those with divers diseases", at sunset; St. Luke alone writes, "He laid his hands on everyone of them and healed them", again bringing out the method of cure.

In the account of the demoniac in the country of the Gadarenes, St. Luke alone says that the man had been possessed for a "long time", also that he "ware no clothes", both details which a medical man would note in a case of this sort. It is true, however, that St. Mark does add, after describing the cure, that the man was "clothed and in his right mind".

In describing the healing of the woman which had an issue of blood, the Greek word (ἴσταναί) used by St. Luke to describe the cure has a purely medical sense, and is used nowhere else in the New Testament in the same way. There is another peculiarity in this account. St. Mark reads:

> "And a woman which had an issue of blood twelve years, and had suffered many things of many physicians, and had spent all that she had, and was nothing bettered, but rather grew worse. . . ."

But St. Luke says:

> "And a woman having an issue of blood twelve years, which had spent all her living upon physicians and could not be healed of any. . . ."

He admits that medicine had failed to help the woman, but quietly passes over St. Mark's perhaps natural implication of resentment at the failure.

The striking off of Malchus' ear by one of those trying to protect Christ is described in all four Gospels, but only St. Luke tells us of the man being healed by Our Lord.

Then there is the account of the woman

> "Which had a spirit of infirmity eighteen years, and she was bowed together and could in no wise lift herself up. And when Jesus saw her he called her to him and said unto her, Woman thou art loosed from thine infirmity. And he laid his hands upon her and immediately she was made straight and glorified God."

The Greek word for "lift herself up" is the same as that used by Galen for straightening of the spine. The term used for "thou art loosed" occurs nowhere else in the New Testament in this sense. It is applied by medical writers, such as Hippocrates, Aretæus, etc., to releasing from disease, relaxing tendons, and taking off bandages. The whole passage shows the medical observation that one might find in a case report. The length of her illness is noted, and then the stages of recovery, such as the relaxation of the muscles and contracted joints, followed by the straightening of the spine.

The Parable of the Good Samaritan; this is found only in St. Luke, and, as Dr. Hobart says, it would have been likely to attract him

on account of its medical aspects. It was not unusual for persons seized with illness on a journey to take refuge in inns. Galen speaks of it, and quite possibly Luke had attended travellers in like case himself. The word describing the man as being "half dead" is used by Galen and occurs only in St. Luke. Also, he uses the Greek work "trauma" (τραῦμα) for the "wounds". This is a technical word frequently used in medical circles nowadays. Elsewhere in the New Testament if wounds are referred to a different Greek word (πληγή) is employed.

Two examples may be taken from the Acts. In the healing of the lame man by St. Peter at the gate of the Temple "which is called Beautiful" the details are given in definite medical language. The cure is described as follows:

"And he took him by the right hand and lifted him up; and immediately his feet and ancle bones received strength, and he, leaping up, stood and walked."

The Greek word for "feet" (βάσις) is peculiar to St. Luke, and showed that he went into the exact nature of the man's disease. The word was used by medical writers then just as "base" of the skull is used by us now. The word for "ancles" (σφυρά) is purely technical, and one would expect only a trained medical man to know about it.

The other example is in the account of St. Paul being bitten by the viper on the island of Malta. The verse reads:

"And he shook off the beast into the fire and felt no harm. Howbeit they looked when he should have swollen up or fallen down dead suddenly."

The word for "swollen up" was the usual medical term for inflammation, and that for "falling down" was used in connection with falling in an epileptic fit, or from severe injuries.

These few examples show quite clearly how familiar Luke was with the technicalities of a medical training. Several more could be adduced. But in addition to these there are certain general characteristics in his writing which unmistakably indicate the medical point of view. These appear partly in his comments, and partly in his using some medical phrases much more frequently than do the other Evangelists, for of course they also employed some.

It is Luke alone who mentions, in the story of the man with the withered hand, that it was his right hand, a detail of no special significance, but evidence of keen observation. And of the leper who was healed, his description means that the man was full of leprosy, a very bad case.

In the case of the healing of the boy with epileptic seizures, Luke's account reads:

"And behold a man of the company cried out, saying, 'Master I beseech thee to look upon my son, for he is mine only child' ".

The boy had already been brought to the disciples, but without avail. Luke uses a Greek word for "look upon my son" which had the sense in medical writings of examining the appearance and condition of the patient, as if the man was appealing to Our Lord to consider the case afresh. He also adds the touch of pathos in the sentence "for he is mine only child".

Again, in recording Our Lord's saying "It is easier for a camel to go through the eye of a needle, etc.", Matthew and Mark both have almost the same words, but the needle is described in St. Luke by a word which meant the needle used in surgical operations; it appears commonly in Hippocrates and Galen. And the word for the eye of the needle was the accepted medical term for perforations in the body, such as the ears, the sockets of the teeth, etc.

Then there is Our Lord's saying "They that are whole need not a physician." Matthew and Mark use a word meaning "whole" or "strong", while Luke has a different term, with the medical significance of "being in good health".

The variety of words employed by St. Luke for the beds of the sick is remarkable. He uses four altogether. Two of these are common to him with the other Evangelists, namely, κλίνη the general word for a bed or couch, and κράββατος, the pallet of the lower classes. The other two are peculiar to himself, and both are diminutives of κλίνη, meaning small, light couches or litters for carrying the sick. This was the kind of bed on which the man was let down through the hole in the roof to be cured by Our Lord.

In the account of the scene in the high priest's palace on the night when Our Lord was seized, Mark says that one of the maids seeing Peter warming himself at the fire, "looked upon him" and then denounced him. In St. Luke, however, the account reads "looking steadfastly upon him", and the difference is that the Greek word here is that which was employed by medical writers to denote a peculiar fixed stare.

The description of the Agony in the Garden of Gethsemane bears the strongest possible characteristics of medical writing, especially when compared with the accounts in Mark and Matthew, which are similar to each other, but do not have the details added by St. Luke. He describes the prostration and the outward and visible effects on his frame of the inner anguish of Our Lord:

"And there appeared unto him an angel from heaven, strengthening him."

The word for "strengthening" is found only in St. Luke and in the Hippocratic writings: it means "to impart physical strength."

"And being in an agony, he prayed more earnestly."

The word for "agony" is peculiar to St. Luke, and had the medical sense of a paroxysm of the most intense suffering.

"And his sweat was as it were great drops of blood falling down to the ground."

All the terms used here are peculiar to St. Luke and bear special medical connotations.

"And when he rose up from prayer and was come to his disciples he found them sleeping for sorrow, and said unto them, 'Why sleep ye: rise and pray'."

Even in accounting for the sleepiness of the disciples Luke adds his own touch in saying that they slept "for sorrow", or "anxiety". The other Evangelists merely say "for their eyes were heavy."

Similarly, in Acts 20: 9-12, when he describes the scene in the upper chamber on the eve of St. Paul's departure, he shows how the youth Eutychus, sitting in the window, was gradually overcome by the heat and weariness, for, as he says, "there were many lights in the room", and the service was long. The passage reads:

"And there sat in the window a young man named Eutychus, being fallen into a deep sleep; and as Paul was long preaching, he sunk down with sleep, and fell down from the third loft, and was taken up for dead."

The term applied to the sleep was a strictly medical one, and by the manner in which it is twice used in this passage different degrees of sleep are indicated, first the dropping off and then the complete relaxation and loss of muscular control. Nowhere does Luke write with keener descriptive powers.

I have taken only these very few instances to illustrate my point. Nearly 400 words or phrases of the kind have been collected by Dr. Hobart, and if some of them seem to be a little forced in their application, there are still more than enough to indicate the medical training of the man who used them.

A late tradition supposes Luke to have been a painter of some skill. There is a supposition also that he was one of the seventy disciples, and that he was one of the two who journeyed to Emmaus with the risen Lord. He alone relates the account of this journey, and he does so in such a graphic manner as to make it likely that he was an eye-witness. Special attention is also drawn to the fact that he leaves the name of one of the disciples unmentioned.

St. Luke was of course a fellow-labourer with St. Paul, joining him at Troas and going with him to Macedonia, and later to Rome. It is possible (how much one would like to be able to say, it is certain) that St. Paul was referring to Luke when he wrote to the Corinthians (2 Cor., 8: 18),

"And we have sent . . . . the brother whose praise in the Gospel is spread through all the churches."

He accompanied St. Paul to Rome and remained with him to the end. We know nothing more of him.

What can we learn of his personality from his own writings? Nothing directly. But his qualities of self-effacement, of sympathy with distress, of sensitiveness of mind, of appreciation of poetry and the music of words, are all plain to us. These things, however, admirable in themselves, still do not tell us all. It is St. Paul who puts him before us in his full stature. He was the beloved physician, and he was loyal to the last. Who would desire a finer memorial?

Association Notes

THE 1939 ANNUAL MEETING IN MONTREAL

Arrangements have been completed to hold the Annual Meeting of the Canadian Medical Association in Montreal in June, 1939, after an absence from this city for ten years. As in 1929, the Windsor Hotel has been chosen as convention headquarters.

Several features promise to make this meeting an outstandingly successful one. Although the program will in the main follow the arrangement of previous meetings, an innovation unfamiliar to Canadian medical conventions will be introduced. Each morning, between 8.30 and 9.25, Round-table Conferences in Medicine, Surgery, Obstetrics, Pædiatrics and Oto-Laryngology will be held. At each conference (and each specialty will hold several), some definite topic will be taken up. Those who attend are free to ask any question they please which is related to the subject under discussion. No *paper* will be given during the hour; the whole time will be devoted to questions, answers and discussion.

To most of those who attend the Annual Meeting is not only an opportunity to acquire

MONTREAL HOTELS

DAILY RATES - EUROPEAN PLAN

	Single room without bath	*Single room with bath*	*Double room without bath*	*Double room with bath*
Windsor Hotel....	Nil	$4.00	$4.50	$7.00
Mount Royal Hotel	Nil	4.00	4.50	7.00
Ritz-Carlton Hotel	Nil	5.00	Nil	8.00
Queen's Hotel.....	$1.50 & 2.00	2.50 to 3.50	3.00	3.50 4.00 4.50
Berkeley Hotel....	Nil	3.00 3.50	Nil	5.00 6.00
Hotel De LaSalle..	Nil	3.00 3.50	Nil	4.00 4.50
Ford Hotel.....	1.50 & 1.75	2.00 to 2.50	2.50 & 2.75	3.00 to 5.00

scientific knowledge, but also a happy vacation away from the cares of practice. Committees are busy on plans to entertain the visiting doctors as well as their wives and the young people who accompany them. June is the most pleasant month of the year in Montreal. Then, the trees, parks and gardens, both public and private, are at their best. The days are warm enough for every outdoor sport, and the evenings cool enough to permit of the enjoyment of the indoor diversions associated with the life of a large city.

The principal hotels are all within easy walking distance of the Windsor where all the meetings will be held.

The Cancer Campaign

The Canadian Society for the Control of Cancer

Proceeding according to the plans outlined at the first meeting of the Grand Council in Toronto on November 1st, the Society is pleased to report progress in its campaign of public enlightenment. Three public addresses were delivered in Toronto during November by a medical speaker. Two were given before women's organizations and one before an audience of both men and women. The attendance at these meetings was approximately 500, 300 and 100. Great interest was shown, particularly in the questions and discussion following the papers. The importance of early diagnosis and adequate treatment was emphasized and the fact that cancer can be cured if treatment is sought when it is still a local disease was stressed. Great emphasis was placed upon the fact that early cancer in the great majority of cases is not associated with pain. Some of the signs and symptoms of early cancer in various parts of the body were enumerated, and a strong appeal made for the necessity of seeking competent medical advice upon the slightest suspicion of the existence of any of these clinical features.

It is felt that talks such as these will ultimately result in patients going to their doctors for advice earlier than has hitherto been the custom. It is realized that some may go who have not cancer, but this is unavoidable. The medical profession, it is believed, is quite capable of dealing with this problem. Nevertheless, every practising doctor must be alert and exercise great care in every examination in order that admissible errors in diagnosis shall be kept to a minimum. If and when suspicion is aroused in a given case facilities are usually available whereby the diagnosis can be made. This may necessitate a biopsy, and if so it should be performed. In fairness, however, to the patient and to the doctor who is going to assume the responsibility of providing adequate treatment for this ruthless malady it should be performed by the one who is going to treat the patient. All possible methods of treatment should be carefully considered and a definite complete plan decided upon before even a biopsy or any other apparently trivial procedure is undertaken.

In dealing with cancer there is no place for a policy of "wait and see." The time factor is of paramount importance, and upon the shoulders of the doctor first consulted rests the responsibility of not only advising appropriate action but of using every means within his power to see that his advice is followed forthwith.

In view of the results of treatment in recent years, instead of adopting a pessimistic attitude concerning this disease, there is much to warrant a spirit of optimism and confidence.

Under the auspices of the Nova Scotia Branch a large public meeting was held in Halifax on December 8th. Dr. A. Primrose, F.R.C.S., F.R.C.S.(C.), Professor Emeritus of Surgery, University of Toronto, the speaker for the evening, gave an inspiring address. Other speakers were Mr. R. V. Harris, K.C., President of the Nova Scotia Branch and C. C. Ross, M.D., F.R.C.S.(Edin.), Executive Secretary of the Society.

In January a public meeting is to be held in Ottawa. This is being arranged by Unit number One of the Ontario Branch of the Society, and promises to be an outstanding success.

The first issue of the Society's Bulletin will make its appearance in January. Under the capable guidance of Mr. H. Napier Moore, as Editor-in-Chief, a very worthwhile periodical is anticipated.

Repeatedly favourable comments are received concerning the value of the "Handbook on Cancer" prepared by the Authorship Committee of the Department of Cancer Control of the Canadian Medical Association.

The Society needs the active support of every practising physician. Knowledge of the Canadian medical profession leads one to believe that full cooperation in every way can be expected by this organization which was sponsored by the Canadian Medical Association.

C. C. Ross, M.D., F.R.C.S.(EDIN.).
Executive Secretary.

Cancer in Ontario

This is a statistical review of the cancer problem in Ontario, where this disease ranks second as a cause of death, being responsible for 11.8 per cent of all deaths. The death rate rises rapidly with age—60 per cent of deaths under 70 years and 34 per cent under 60 years are due to cancer. More than half the deaths are attributable to cancer of the digestive system. In females cancer of the breast ranks first in numerical importance, in males, gastric cancer. In over a quarter of all cases the primary cancer is "accessible." The general evidence suggests that incidence of cancer is not increasing, and that one-third of the apparent increase may be

attributed to "ageing" of the population.—*Canad. Pub. Health J.*, 1938, **39**: 387. Abs. in *Brit. M. J.*

Government versus Cancer

In announcing the Government's decision to make available modern facilities for the diagnosis and treatment of cancer in this country at the Council Dinner of the British Medical Association on November 8th Dr. Walter Elliot, the Minister of Health, said that in elaborating the details of the scheme he undertook to do his utmost to consult all the interests concerned—"local authorities, medical practitioners, research men." Later it was announced that Dr. Elliot was in negotiation to purchase £500,000 worth of radium for the treatment of cancer, and, according to a statement in the *Times*, the Eldorado Gold Mines, Ltd., at Port Hope, Ontario, have received an order from the British Government for 11 grams of radium at a cost of about £200,000. That the Government has taken this important step is to be warmly welcomed by the medical profession, and it is much to be hoped that the Minister has fulfilled or is fulfilling his promise to consult those experts who alone are in a position to give him the best advice as to what could be expected from any scheme planned on the scale contemplated. Has, for example, sufficient cognizance been taken of the developments in radiotherapy in other countries? It is the opinion of many distinguished workers abroad that in future radium will be used only for implantation into the actual growth, and that x-rays will be employed for attack on those deeper growths which are inaccessible to direct implantation methods. This opinion requires the most careful examination before any irrevocable step is taken. Results obtained by expert and careful application of "bombs" containing 5 grams of radium are encouraging enough to justify their use in the treatment of growths only a few centimetres below the surface of the skin. But for the deeper growths, as, for example, in the lung, stomach, and rectum—"bombs" containing as much as 20 grams would be needed, and it is obvious that not many of these would be available at the present price of radium. Here it may be pertinent to remark that with the development of the radium mines in Canada it does not seem at all unlikely that within a few years the price of radium may be considerably less than it is now.

Coincident with this development in the mining of radium is the work started by Professor E. O. Lawrence in the University of California with the cyclotron, which has been described as an "atom smasher". Already in the United States twenty-two of these machines are in operation or are being built; several are under construction in the Scandinavian countries, and at least two of these will be used partly for medical and biological purposes. The two machines that are being built in this country at Cambridge and at Liverpool will be devoted largely to physical work and are not designed for use in medical treatment. We have already drawn attention in these columns* to the cyclotron and to the fact that the artificially radioactive substances produced by it have been given to patients suffering from myelocytic leukæmia, with successful results. A team of workers in the University of California is now actively engaged in investigating the possibility of substituting neutrons for radium in the treatment of cancer. Neutrons have been shown to be at least three times more lethal to malignant cells than an equal dose of x-rays. It is clear, then, that the production of artificially radio-active substances and of neutrons by the cyclotron in amounts that make them easily available for therapeutic purposes is of the highest importance. The question immediately arises: Has the Minister of Health gone into this question and discussed with expert medical advisers the possibility (we would say desirability) of developing a cyclotron unit in this country exclusively for medical purposes? Is it indeed too late to suggest that say one-tenth of the £500,000 might be set aside for this end? While radium is needed and of great value in the treatment of cancer, it is essential that other methods of treating this disease—and especially the newest methods—should not be neglected. A cyclotron unit for medical research is urgently needed, and there are men with the necessary technical training and experience to operate it. We would suggest, too, that if the building of this apparatus should come to form part of the Government's cancer scheme, then research with it should be under the guidance of some such authoritative body as the Medical Research Council. It is essential that research be not neglected.—Leading Article, *Brit. M. J.*, 1938, **2**: 1091.

Medical Societies

The Cumberland County Medical Society

The Cumberland County Medical Society held its annual meeting at Oxford, N.S., and officers for the ensuing year were elected: *President*, Dr. F. E. Walsh, Springhill; *Vice-president*, Dr. David Drury, Amherst; *Sec.-treasurer*, Dr. J. W. Sutherland, Amherst; *Representatives* to the Nova Scotia Medical Society, Drs. C. A. MacQueen, Amherst and J. R. Gilroy, Oxford.

The District of Beauharnois Medical Association

A new medical society was formed in December with a nucleus of members of the Canadian

* *Brit. M. J.*, 1938, **2**: 25.

Medical Association. It is called the District of Beauharnois Medical Association. The officers are as follows: *Hon. President,* Dr. J. C. Moore, Huntingdon, Que.; *President,* Dr. H. R. Clouston, Huntingdon; *First Vice-president,* Dr. M. R. Stalker, Ormstown; *Second Vice-president,* Dr. O. E. Caza, Valleyfield; *Sec.-treasurer,* Dr. C. L. Roman, Valleyfield.

The Royal College of Physicians and Surgeons of Canada

The Ninth Annual Meeting was held in the auditorium of the National Research Council, Ottawa, on October 29, 1938. Dr. George S. Young, President, occupied the Chair and some 120 Fellows registered.

The President presented the report of the activities and decisions of Council during the past year. Two meetings had been held, one in Halifax in June, with attendance of 14 and one in Ottawa (2 sessions) at the time of the annual meeting, with an attendance of 23. The total strength of Council is 27.

The following candidates were successful in passing the Primary Examinations and are entitled to a certificate: Yvette Brissette (Miss), 19 Moncton Ave., Quebec; Jean M. Grandbois, 127 Grande Allée, Quebec; André Jacques, Sainte-Marie, Comté de Beauce, Que.; Laurent Pesant, Ste. Dorothée, Comté Laval, Que.; Joseph J. Cholette, 1451 Boulevard St. Joseph, Montreal; Gerald C. Bowes, 647 Milton St., Montreal; John C. Dickison, 4462 Western Ave., Westmount, Que.; Alfred E. Hill, 142 Union Boulevard, St. Lambert, Que.; John D. Stenstrom, M.D., Montreal General Hospital, Montreal; John W. Babb, 410 St. James St., London, Ont.; David J. Breithaupt, 166 Margaret Ave., Kitchener, Ont.; Lloyd Hisey, 12 Fallingbrook Crescent, Toronto; Howard G. Kelly, 397 Brock St., Kingston, Ont.; Kenneth C. King, 290 Huron St., Toronto; Robert L. MacMillan, 28 Admiral Road, Toronto; John G. P. Mickler, 41 Tyndall Ave., Toronto; Benjamin F. Guyatt, 53 Harbord St., Toronto; James A. Romeyn, 83 Spadina Road, Toronto; Roderick C. Ross, Vineland Station, Ont.; John W. Scott, 44 Russell Hill Road, Toronto; John G. Stapleton, 386 John St. N., Hamilton, Ont.; David State, 48 Kains St., St. Thomas, Ont.; Morris Stein, 226 Niagara St., Toronto; Frederick F. Sypher, R.R. No. 8, London, Ont.; George R. Walker, 67 St. Clair Ave. E., Toronto; Thomas S. Wilson, 63 Celebration St., Saint John, N.B.; James F. Elliott, M.D., University of Alberta Hospital, Edmonton; Anathalie W. Heath (Miss), 10122 - 124th St., Edmonton.

The following candidates were successful in passing the final examination to qualify for Fellowship: *Division of Medicine.*—Drs. John Wendel MacLeod, Montreal; Lloyd W. Thompson, Weston, Ont. *Division of Surgery.*—Drs. John W. Merritt, Halifax; Paul Bourgeois, Montreal; Jean Tremblay, Montreal; Eric A. MacNaughton, Temiskaming, Que.; Robert A. Johnston, London, Ont.; W. W. Moffatt, Port Colborne, Ont.; Samuel V. Railton, Port Colborne, Ont.; Christopher M. Spooner, Toronto; Thomas Stewart Perrett, Toronto.

Ad Eundem Fellowships have been granted to: Drs. Leon Judah Solway, M.R.C.P.(Lond.), Toronto; John Hammond Palmer, M.R.C.P. (Lond.), Montreal; George Alexander Davidson, M.R.C.P.(Lond.), Vancouver; Robert Andrew Hunter, M.R.C.P.(Lond.), Victoria, B.C.; Samuel Edward Caldbick Turvey, M.R.C.P. (Lond.), Vancouver.

The next annual meeting will be held in Ottawa on Saturday, October 28th—and the 1939 examinations will be held in the month of October as heretofore, with Halifax and Toronto as the centres for oral and clinical examinations. In addition a special examination, written and oral in the primary subjects, for English-speaking candidates, will be held in Montreal in June, 1939. Examinations in the French language will be conducted in October as heretofore, with Montreal and/or Quebec the centre for oral and clinical examinations.

The regulation was made mandatory that a candidate failing to pass the written examination shall not be permitted to present himself for the oral or oral and clinical portion of the examination.

Progress has been made in the study of a plan for the certification and registration of specialists. The College will apply to the Federal Legislature for amendment to its charter authorizing the exercise of that duty.

The Scientific Session was of unusual interest, being contributed to by Professor Wm. Boyd, Toronto, on "Some etiological factors in cancer"; Dr. E. W. Archibald, Montreal, and Sir Frederick Banting, Toronto, on "Various aspects of cancer research". The day was closed by the Annual Dinner which proved to be a delightful affair, with His Excellency Lord Tweedsmuir as guest speaker.

The text of His Excellency's address follows.

I need not tell you, gentlemen, that I am glad to be here tonight. I am always happy in the company of your profession, and I am proud to be an honorary Fellow of your two Colleges of Medicine and Surgery. For two months this autumn I was very much in medical society, for I had a rest and a "cure" in a famous clinic among the Welsh mountains. I arrived in England this summer very tired, and after a strenuous fortnight of interviews and speeches and discussions I was dog-tired, so Lord Dawson promptly despatched me to a place where I was under discipline and had nothing to do except to get well. It was an experience of which I can only say that I enjoyed every moment, and I especially enjoyed the company of the distinguished doctors and specialists attached to the institution.

So I came to reflect a good deal upon medical science, and I venture to offer you a few of these reflections tonight. When I observed the careful, patient and precise curative work going on around me I realized how well-deserved was the reputation of your profession. That reputation has been high ever

since the time of Hippocrates and Galen, and it has never been higher than today. If you will look at the statute of Henry VIII which confirmed the Letters Patent establishing the Royal College of Physicians in England, you will find that none were "to be suffered to exercise and practice physic but only those persons that be profound, sad and discreet, groundedly learned and deeply studied in physic." I am very certain that the company here tonight is profound and discreet and deeply learned, but I am glad to think that it is not sad.

Not only has your profession always been admired, but it has been always popular. A proof is that it is the subject of many jokes. Human nature does not joke about anything which it fears or dislikes. It would be possible to make an amusing anthology of gibes at the sacred art of healing. There is, for example, the sentence of Rousseau— "Live according to nature and never mind the doctors. That will not prevent you dying, but it will prevent you dying more than once." The other day in a *Life* of Sydney Smith I came on one that was new to me. He was staying in a country house at a shooting party, and after the day's shoot an eminent physician came in in a bad temper. "I shot scandalously," he said, "at the last stand. I hardly killed any birds." "My dear fellow," said Sydney Smith, "why didn't you prescribe for them?" That kind of ribaldry is the homage which ignorance pays to skill, skill for which it has a real affection. It is a common phrase, "a beloved physician". Did you ever hear people talk of a beloved solicitor or a beloved electrical engineer?

At the same time, medical science has always had a certain aura of mystery about it. In the Middle Ages a doctor was not a man to be trifled with, for he had uncanny powers at his call. He might be a good man, but he was not supposed to be always too good a Christian. You remember the description of the doctor in Chaucer's *Canterbury Tales*— "His studie was but litel on the Bible". A physician was a master not only of strange drugs but of spells and incantations.

Those days are long gone, but there is still a certain atmosphere of mystery about your craft. The ordinary man may have a smattering of divinity or a smattering of law, but as a rule he knows very little about medicine. Now that is both a good and a bad thing. It is a good thing, for it makes sensible people put themselves in a doctor's hands when they are sick, and do what he tells them, since they recognize their ignorance; it is a bad thing for it opens the door to the quack and the charlatan.

So tonight I am going to make two suggestions to you, the suggestions of a layman, made with all deference and modesty. The first is this. I believe it would be an excellent thing if your profession saw that the ordinary public had some elementary instruction in the rudiments of medicine. It need not be deep. It need concern itself only with the most general principles, and it should be directed to the prevention of needless anxieties and false hopes. If, for example, it were firmly rooted in the popular mind that something out of a bottle will not cure cancer, then a good many quacks and patent-medicine vendors would go out of business. Again, long experience has made us pretty familiar with certain common ailments, but there appears to be a host of new diseases, mysterious affairs with which the ordinary man is completely unfamiliar, and which in consequence he dreads. *Omne ignotum* is not only *pro magnifico* but also *pro horrifico*. I find in many quarters something very like panic when certain diseases are mentioned such as infantile paralysis and sleeping sickness and streptococcus infection. I believe that much could be done to steady the popular mind if your profession were prepared to give a little elementary instruction on such subjects.

My second and final suggestion is a sentence of Plato written two thousand years ago. Here it is— "This is the greatest error in the treatment of sickness, that there are physicians for the body and physicians for the soul, and yet the two are one and indivisible." There is a profound truth in that saying. More and more today we realize the close interconnection between mind and body. The nerves play a prominent part in most ailments, and in most cases the nerves represent a condition of mind. Hygiene and therapy should cover the whole area of human needs, and the doctor must have an eye to the spiritual as well as to the physical make-up of his patient. It is not enough to have specialists for mental diseases and specialists for physical diseases; the same man must in a sense be both. A good doctor should be—and indeed always has been—something of a psychologist. I remember hearing Lord Horder once say that the first textbook of medicine should be a primer of logic. And I personally should always distrust the psychologist who had not a considerable knowledge of medical science.

There, gentlemen, you have my reflections this autumn, in the intervals of being x-rayed and dieted among the Welsh hills. I am glad to say that I have come back to Canada greatly fortified in body and mind, and looking eagerly forward to the two years' sojourn which remain to me.

Topics of Current Interest

Regulations in the United States Governing the Prescription and Sale of Cannabis Indica

Regulations for effectuating the provisions of the Marihuana Tax Act of 1937 were approved September 29 by the Secretary of the Treasury. The general requirements of the Act as they relate to physicians were stated in the Organization Section of the Journal, September 11, pp. 31B and 32B. Every physician who distributes, dispenses, gives away, administers or prescribes cannabis or any of its derivatives or preparations is required by the Act to register with the collector of internal revenue of his collection district, obtain an official registration number, and pay the required tax.

Applications for registration must be filed on form 678c, procurable from the collector of internal revenue. An inventory, in duplicate and under oath, of all cannabis and preparations thereof on hand must be filed with the application. Physicians will normally register in class 4 and be subject to a tax of $1 each year. A physician who sells or dispenses cannabis apart from the legitimate practice of his profession is liable to an additional tax of $3.00 a year as a dealer. If he dispenses cannabis only incidentally to the legitimate practice of his profession he incurs no liability for the tax imposed on the dealer. A physician maintaining an office in a collection district where he is duly registered with the collector of internal revenue and where his stock of cannabis and his cannabis records are kept may, but only in the course of his professional practice, distribute, dispense, give away, administer or prescribe cannabis in other collection districts in which he lawfully engages in the practice of his profession, without incurring additional tax liability; but if he maintains an office in another collection district or even maintains two or more offices in the same col-

lection district, he must pay a tax with respect to each office.

Hospitals, colleges, medical and dental clinics, sanatoriums and other institutions, not exempt as government institutions, are subject to the same taxes and incidental regulation as other registrants similarly dealing in or handling cannabis. When an institution is subject to tax, the head thereof or of the department wherein the cannabis is to be used must sign the application for registration. Nurses, under the regulations, are regarded as agents of the practitioners or institutions under whose direction or supervision their duties are performed. They are not permitted to register under the Act nor are they permitted to be in possession of cannabis except as such agents or as patients. Cannabis left by a physician with a nurse, to be administered during his absence, must on her discharge from the case be returned to the physician, who will account for it on his records. Any cannabis found in the possession of a nurse not at the time under the supervision of a physician will be forfeited to the government.

A physician desiring to obtain cannabis must make application on form 679a (Marihuana), to the collector of internal revenue for the district in which the physician is located for the purchase of an order form. The application must show (1) the physician's name, address and cannabis registry number, (2) the name and address of the person from whom the cannabis is to be purchased, and (3) a description of the desired cannabis and the amount to be purchased. The application must be accompanied by a certified cheque, cash or money order in payment of the transfer tax of $1.00 an ounce or fraction thereof, plus 2 cents in payment of the order form. Order forms will be prepared by the collector in triplicate. The original and duplicate will be delivered to the physician. He will deliver the original to the person from whom he purchases the cannabis and preserve his duplicate copy for two years. The triplicate will be retained by the collector. There are no exempt medicinal cannabis preparations; every preparation containing cannabis in any form and in any amount is covered by the Act. Physicians must keep daily records showing the kind and quantity of cannabis dispensed or administered, the name and address of each person to whom dispensed or administered, the name and address of the person on whose authority the cannabis was dispensed or administered, and the purpose for which it was dispensed or administered. Every such record must be kept for a period of two years in such manner as to be readily accessible to inspection by investigating officers. No special record form will be furnished by the government for the use of those registered as practitioners, including hospitals and institutions, but each registrant is advised to keep records in the manner that is best calculated to enable an inspecting officer quickly to ascertain the quantity and kind of cannabis used daily. The initials of the practitioner giving directions for the administering of cannabis to a patient in a hospital should appear on the patient's record chart, or a prescription may be used, giving the name and address of the patient, the date, and the physician's signature or initials, which should be filed with the pharmacist in charge of the drug room before the cannabis leaves his charge. If, however, a prescription is used, reference to it should appear on the chart.

All prescriptions for cannabis must be dated as of and signed on the day when issued, and must bear the full name and address of the patient and the name, address and cannabis registry number of the practitioner. Prescriptions should be written with ink or indelible pencil or be typewritten. If typewritten, the prescription should be, of course, signed by the physician. The refilling of a prescription for cannabis is prohibited by the regulations. Generally, the the furnishing of cannabis pursuant to telephone advice of physicians is prohibited, whether prescriptions covering such orders are subsequently received or not. In an emergency, however, a dealer may deliver cannabis through his employee or responsible agent pursuant to a telephone order, provided the employee or agent is supplied with a properly prepared prescription before delivery is made, such prescription to be turned over to the dealer and filed by him as required by law within a reasonable time after delivery. The government does not furnish prescription forms. Any form may be used, provided it is properly executed and shows the required information.

A physician who utilizes cannabis in the course of his professional practice should obtain a copy of the regulations that have been promulgated and familiarize himself with their requirements. Application for such a copy may be made to the collector of internal revenue of the collection district in which registration is to be effected.—*J. Am. M. Ass.*, 1937, **109**. Prepared by the Bureau of Legal Medicine and Legislation.

Medico-Legal

Protection of Medical Witnesses

The question of the protection of medical witnesses is discussed in a recent number of *The Lancet* (July 23, 1938) in reference to a decision in a medico-legal case several years ago. A married woman, Mrs. M., in trying to obtain a separation from her husband on the grounds of alleged cruelty, consulted the late Sir Patrick Watson, M.D., to obtain his testimony with regard to her broken-down condition which she contended was due to her husband's ill-usage. Two years later she brought her action for separation, and was again medically examined by Sir Patrick, but this time on behalf of the husband. Sir Patrick reported the results of

his examination to the husband's solicitors, and also mentioned what he had learnt from his previous examination of her, showing his private notes made at the time. When later on he was called as a witness for the husband, he gave this information in evidence, producing his private note-book in which he had recorded his opinion that Mrs. M. (then pregnant) should be weaned of her morphia habit and kept in a nursing home till the birth of the child. He felt that induction of premature labour was being sought.

Mrs. M. lost her case, and she thereupon brought action against Sir Patrick Watson on the ground that he had committed a breach of his duty of secrecy in showing his notes to the solicitor or in voluntarily giving evidence of their contents. She also claimed that the notes were defamatory in imputing to her a desire to procure criminal abortion.

Her counsel, the late Lord Haldane, argued that a medical man having received a fee for visiting his patient for the purposes of her own litigation and having obtained information for her benefit was not at liberty to disclose that information to the other side. In addition he held that the protection of a witness did not extend to his attendance at a solicitor's office when he was interviewed for his evidence.

The Lord Chancellor, however, would give no ruling on this aspect of the confidential relationship between patient and medical man. He held that it was much more simple to decide the case on the ground that a witness's statements in court are absolutely privileged. Whatever a prospective witness says to a litigant or a litigant's legal advisers is equally privileged, otherwise witnesses would not give any information to their counsel beforehand for fear of being sued. Witnesses, said the Lord Chancellor, are immune. The only remedy against them is to indict them for perjury if they do not speak the truth. In the case of Sir Patrick Watson there was no question of his having communicated anything to strangers or to persons outside of the litigation.

The question arose however whether Mrs. M. had a genuine grievance in the fact that her professional adviser, to whom she had appealed for help, had helped her opponents: might he not have abstained from supporting her claim without voluntarily assisting in checkmating it? Here again Lord Halsbury was similarly outspoken. "If" said he, "he is a person engaged in the administration of justice, on whichever side he is called, his duty is to tell the truth and the whole truth: if he does this duty it matters not on which side he is called."

The Lancet concludes, reflectively, with the remark that as a matter of professional tradition rather than of legal protection, circumstances can be imagined in which the medical profession would not unanimously approve the disclosure by a physician of his patient's confidence. H.E.M.

Abstracts from Current Literature

Medicine

Observations on the Continued Use of Protamine Zinc Insulin in Patients with Severe Diabetes Mellitus. Ralli, E. P., Fein, H. D. and Lovelock, F. J.: *Am. J. M. Sc.*, 1938, **196**: 28.

The authors are reporting a group of 20 patients with diabetes mellitus from the clinic of the Bellevue Hospital, New York City. Sixteen of the 20 patients were studied for periods of not less than 8 months while receiving protamine zinc insulin. The other 4 were observed for 1 to 2 months in the hospital, at the end of which time protamine zinc was discontinued owing to the fact that it was impossible to prevent a significant degree of glycosuria. All of the reported cases had previously been under observation and treatment in the clinic for an equal or longer period of time on soluble insulin. In the case of the remaining 16 patients whose diabetes could be temporarily controlled on protamine zinc insulin it was found necessary after 8 months of protamine zinc therapy to return 7 of them to soluble insulin because of the occurrence of alternating periods of uncontrolled glycosuria and insulin shock. Of the remaining 9, eight required soluble insulin as well as protamine insulin in order to control the diabetes. Those patients who were successfully treated by means of the protamine zinc insulin were found to have low basal metabolic rates. The authors suggest that lowered thyroid activity may render such more sensitive to the action of insulin. Thus the more slowly absorbed insulin would be more effective and less of it would be required to control the glycosuria. E. S. MILLS

Studies in Diabetes Mellitus. VI. Mortality and Longevity of Diabetics. Joslin, E. P., Dublin, I. I. and Marks, H. H.: *Am. J. M. Sc.*, 1938, **195**: 596.

This paper covers the total experience on all true diabetics treated by Joslin and his associates between the years 1897 and 1928. Follow-up efforts were limited to special groups of patients who were of particular significance as illustrating the influence of important factors in the longevity of diabetics. Tabulations were made in the same manner as survivorship experiences in insurance work.

The cases were divided into three groups—those seen in the Naunyn era from 1897 to 1913; the Allen era from 1914 to 1922; and the Banting era from 1922 to 1928. The Banting era was divided in a first part, from August 7, 1922, to 1925, and a second part, from 1926 to 1928. The tables constructed by the authors show that the death rate per 1,000 diabetics of all ages was approximately 217 in the Naunyn era, 152 in the Allen era, dropping to a low of 58 in the second part of the Banting era. The

improvement in the mortality rate was greatest in children. Prior to the discovery of insulin the death rate in juvenile diabetes occasionally exceeded 100 per cent per annum. In other words, the average duration of life in diabetic children was less than one year. With the second Banting era the mortality curve in this group became normal in respect to shape, in that the lowest rates were recorded at younger ages and increased gradually throughout adult life. For instance, the expectancy of life among diabetics aged 10 years prior to 1914 was 1.1 years as compared to 8.0 years at the age of 50, whereas at the present time the expectancy at 10 years of age is 33 years as compared with 13 years at the age of 50. This modern treatment has accomplished more in the younger age groups. The death rates of diabetics are still much in excess of those for the general population. If the normal death rate among persons in the general population at specified periods of time is taken as unity, the death rate in female diabetics of 5 to 14 years prior to 1914 was 263; in the Allen era 147; and in the second part of the Banting era 17. It is therefore evident that the death rate in young diabetics is from 5 to 17 times greater than that for the general population in the corresponding age period. E. S. MILLS

Surgery

Ankylosis of the Temporo-mandibular Joint. Kazanjian, V. H.: *Surg., Gyn. & Obst.*, 1938, **67**: 333.

This is a report based on the continual observation of 33 cases of chronic ankylosis, 28 intra-articular and 5 extra-articular, over a period of several years. The ankylosis may be partial or complete, is usually bony, and allows for less than 5 mm. of opening power or it may be unilateral or bilateral. Congenital anomalies are rare as causative factors, the usual ones being infection and trauma with fibrosis as a sequel and occasionally osteoma. There is always lack of growth in the juvenile cases; whether this is due to injury to the metaphysis, lack of proper function, or the effects of malaligned teeth he does not state. The usual symptoms are due to deformity, limitation of mandibular function and poor mouth hygiene. A mechanical exerciser may be used in some cases of fibrous extra-articular partial ankylosis and in early cases of rheumatoid arthritis, but on the whole they have been of little permanent value; the one he most often uses depends upon the contractile pull of elastic bands. Arthroplasty should be performed early, and this is true in rheumatoid arthritis as soon as it is quiescent. Risdon's exposure was used. The technique is given in detail. Fascia lata, 1½ x 2½ inches, was used as the fascial insert. No complications were severe and dental care was instituted early. After the arthroplasty proper dental care and orthodontic care may be sufficient to provide an efficient occlusion. As a rule correction of the retruded mandible in children should be delayed until the eruption of the permanent bicuspids. He uses oblique section of the mandible from the lingual side of the alveolus combined with traction on the symphysis from a head-band and elastic bands attached to previously prepared dental splints cemented to certain teeth. Extra-articular causes are more difficult in that they present strictly personal problems. For the "unknown" causes he finds the approach below the angle of the mandible of most use. Numerous surgical problems are discussed. FRANK DORRANCE

A Clinical and Anatomical Study of the Semimembranosus Bursa in Relation to Popliteal Cyst. Wilson, P. D., Eyre-Brook, A. L. and Francis, J. D.: *J. Bone & Joint Surg.*, 1938, **20**: 963.

The authors have correlated the descriptions from the standard teaching books on anatomy, the dissection of 30 cadavers, and the findings at 21 operations, and, in roughly 75 per cent, have found that the bursæ under and over the medial head of the gastrocnemius communicated with each other as a composite gastrocnemio-semimembranosus bursa. In 26 dissections the composite bursa communicated with the knee-joint in 15. In cadaver and clinical work they have injected air without untoward results. The causal factor is probably trauma, either as a single violent movement with tear or as repeated small injuries. On the available evidence they reject the hernial protrusion and the ganglion theory. Twenty-nine per cent of the patients were under 15 years, none between 15 and 32, and each decade thereafter was equally represented. In children the chief complaint was swelling; in the older group swelling and slight discomfort, which might have been due to the associated osteo-arthritis present in 7 of the last 11 cases. The authors use aspiration, injection of air, and x-rays preceding the removal of the "Baker's cyst". They use a curved incision with its convexity directed medially, find they have to excise part of the semimembranosus and gastrocnemius to reach the pedicle, which may be narrow but is usually broad, and frequently find they have difficulty in closing it. Complications occurred in only two cases and this post-operative effusion did not cause discomfort. It may be that this composite bursa is of importance in septic arthritis of the knee-joint; in tuberculous arthritis it may explain some of the temporary discomforts following trauma to this part. FRANK DORRANCE

Gonorrhœic Teno-vaginitis. Wilenius, R.: *Acta Chir. Scand.*, 1938, **81**: 195.

This complication occurred in 20 per cent of the joint and tendon complications of gonorrhœa at the Finnish Red Cross Hospital. In 71

acute cases of teno-vaginitis of the flexor tendons (teno-synovitis) 7 per cent were of gonorrhœal origin. The complications arose from 10 days to 5 weeks after the onset of urethritis. The subjective symptoms were much more marked than the objective. The erythrocyte sedimentation rate paralleled the severity; the white blood count averaged 11,000 per c.mm.; the complement-fixation reaction was positive. The author advises immobilization, elevation and heat, with the use of Bier's congestive treatment, roentgen-ray and short wave for the pains. The acute symptoms usually subsided in 2 to 3 days, after which active and passive exercises were instituted. *Restitutio ad integrum* took place in all cases. FRANK DORRANCE

Obstetrics and Gynæcology

Uterine Rupture Following Cæsarean Section. Richards, C. E. B.: *Brit. M. J.*, 1938, **1**: 1359.

Four per cent of Cæsarean scars give way during a subsequent pregnancy or labour. Five groups are described: (1) rupture through an old upper segment incision, with the placenta away from the uterine scar; (2) rupture through an upper segment incision, with the placenta underneath the old scar; (3) rupture after a previous lower segment incision; (4) complete rupture through an upper segment incision, with extrusion of the child but retention of the placenta; (5) complete rupture through an upper segment incision, with extrusion of both child and placenta.

All patients who have been subjected to Cæsarean section should have their subsequent confinements under skilled supervision and within access of a fully equipped operating theatre. Any abnormal symptom, particularly that of lower abdominal pain, must be regarded with suspicion. ROSS MITCHELL

The Experimental Production of Ovulation in the Human Subject. Davis, M. E. and Koff, A. K.: *Am. J. Obst. & Gyn.*, 1938, **36**: 183.

It has been possible for the first time to produce ovulation in women by the intravenous use of a gonadotropic hormone derived from the serum of pregnant mares. This serum has been isolated in such an advanced state of purity that its administration by the intramuscular or intravenous route is devoid of danger, provided that suitable safeguards are established. Biologically, this gonadotropic hormone resembles extracts and implants of the anterior lobe of the hypophysis, but differs chemically and biologically from all other gonadotropic substances heretofore studied.

These experimental ovulations have provided the earliest human corpora lutea yet described. Clinically, this gonadotropic hormone should prove efficacious in the treatment of women in whom follicle growth and ovulation are at fault. ROSS MITCHELL

Hydatidiform Mole: A Statistical and Clinical Study. Chandra Das, P.: *J. Obst. & Gyn. of Brit. Emp.*, 1938, **45**: 265.

The average incidence of hydatid mole change in the placenta in India is 1 in 502, in England, 1 in 835. The average in all hospitals was 1 in 625 pregnancies. This frequency was worked from 222,542 cases including full term and premature labours, miscarriages and abortions. The following causes were enumerated: (1) pre-existing endometritis (Virchow); (2) uterine fibroids; (3) obliterating endarteritis of the vessels of the chorionic villi (Durante); (4) some grave maternal dyscrasia, that is, syphilis, cancer; (5) obscure fetal disease; (6) fetal death; (7) abnormal secretion of the corpus luteum (Fraenkel); (8) effects of emmenagogues (Keiffer); (9) increased activity of the pituitary (Ascheim). Eighty-eight per cent occur in multiparæ. There are two types: (1) hydropic change with little or no proliferation of epithelium; (2) moderate cystic degeneration with actively proliferating syncytium and Langhan's cells. The latter is more frequently followed by chorio-epithelioma. Fifty per cent of hydatidiform moles show bilateral multilocular luteal cysts containing a thin, watery, straw-coloured fluid. Eighty-five per cent of cases showed amenorrhœa for three to five months. Chorio-epithelioma following upon a normal pregnancy is more malignant than that following hydatiform mole. The average incidence, taken from six authors, showed that 20 per cent of hydatidiform moles became malignant. The histological appearance is not a reliable source of the degree of malignancy. P. J. KEARNS

Pædiatrics

An Investigation of the Source of Staphylococcal Infection in Acute Osteomylitis. Williams, S. and Timmins, C.: *Med. J. Australia*, 1938, **11**: 687.

Since the numbers of cases of acute osteomyelitis in the Melbourne Children's Hospital fluctuated from year to year in a way to suggest some relationship with the staphylococcal infections of the respiratory tract, the authors have attempted to relate the strains of the organisms found in the lesions with those found in the respiratory tract of the same children. They note that certain strains of *Staph. aureus* were not cleared to the same extent as others when mixed with staphylococcal bacteriophage. On this basis they recognized six types of *Staph. aureus* and proceeded to classify the organism recovered from the bone lesions, nose and throat, blood antra, skin, etc., in 19 cases of acute osteomyelitis. In 10 of these cases the strain from the bone lesion was identical with that in the nose and throat. In 5 cases the types differed, and in the rest of the cases the investigation was incomplete. While no definite conclusions are drawn from this material, the authors

point out that by this method a proportion of children suffering from osteomylitis can be shown to harbour the same type of staphylococcus in the nose and throat as is present in the bony lesion. REGINALD WILSON

Observations on the Treatment of Empyema in Children. Wallace, H. L.: *Brit. M. J.*, 1938, **2**: 560.

The author reviews the methods of treatment in 363 cases of empyema in children. A sufficient number of cases occurred in each type of treatment to enable comparisons as to results to be made. Under conservative treatment are considered those cases treated by repeated aspiration, canula aspiration and closed suction. The mortality rates in these groups were 38.3, 23 and 28.6 per cent respectively. Under radical treatment are considered groups treated by thoracotomy and open drainage, rib resection with closed suction, and rib resection with open drainage. The mortality in these cases was 29.7, 11, and 11.6 per cent respectively. The total mortality under conservative methods was 30.9 per cent as opposed to 14.9 per cent for radical methods. It must be considered, of course, that conservative methods would be adopted in a greater proportion of very ill infants who were considered poor operative risks. These factors and others are considered and analyzed. It is revealed that success or failure of any form of treatment is governed largely by the age of the child. In this series the most successful method of treatment proved to be rib resection immediately after localization of the empyema by repeated aspiration. The manner of drainage after rib-resection did not appear to have any significant influence on mortality. REGINALD WILSON

Ophthalmology

On a Particular Form of Unilateral Optic Neuritis, Segmentary Neuritis. Bollack, J., Delthil, S. and Offret, G.: *Ann. d'Ocul.*, 1938, **175**: 421.

Optic neuritis has been the subject of numerous classifications, particularly from the standpoint of anatomy, clinical considerations, evolution, and, latterly, etiology. There seem to exist however particular cases that cannot be placed in the usual classification. The observations reported here concern a particular form of unilateral neuritis which differs from the classical types. The symptoms and course in the three cases were very similar, and the symptoms especially seem to the authors to warrant considering them as a definite type. The three cases are described in detail, and while there were some minor differences the resemblances were striking, in that the visual disturbance was in each unilateral, œdema of the papilla was well marked but not prominent, and vascular changes with some juxta-papillary hæmorrhage were present on a section of the disc. In each case the central vision was only slightly affected or normal. The radiological examination was completely negative. Two of the cases however showed slight inequality of the pupils, though none of the patients were syphilitic. S. HANFORD MCKEE

The Treatment of Prolapsed Iris by Trichloracetic Acid (Technique of Bettman and Barkan). Magitot, A. and Dubois-Poulsen, A.: *Ann. d'Ocul.*, 1938, **175**: 449.

Among the complications following the operation for cataract extraction prolapse of the iris is most frequent. In spite of the usual precautions taken to prevent it, the condition at times results. The surgeon under these conditions hesitates to start anew with a further operation, so the procedure of Bettman and Barkan, which coagulates the hernia by trichloracetic acid, deserves to be better known, especially as it gives excellent results. The authors give the details of this method, and cite eleven observations in which it was done, and which confirm entirely the conclusions of the two Americans. It is especially useful in cases with a small prolapse of the iris. While not to be advised in cases with a large prolapse, the result in the small- and medium-sized hernias is quite satisfactory. S. HANFORD MCKEE

Neurology and Psychiatry

Aneurysms of the Circle of Willis. Matas, R.: *Ann. Surg.*, 1938, **107**: 660.

In the brain there are at least three classes of arterial aneurysms which differ in their surgical tractability: (1) The smallest, the most frequent and the most fatal of all aneurysms—the miliary aneurysms of the central ganglionic branches of the circle of Willis, which are responsible for over 80 per cent of the deaths caused by cerebral hæmorrhage. These are entirely beyond the scope of surgery except when they create circumscribed hæmatomata in the brain substance. (2) The larger basal aneurysms of the carotid tracts up to the circle of Willis, which it is possible to control and cure by the extracranial ligation of the internal and common carotid trunks in the neck. (3) An intermediary group of aneurysms arising from the circle and its surface or cortical branches which are not controllable by the extracranial ligation of the parent trunks in the neck. These can be dealt with only by a direct intracranial attack *in loco lesionis* with the view to their extirpation or obliteration by electrocoagulation after occlusion of the pedicle or of the parent trunk with metallic clips, etc., according to circumstances. No operation for intracranial tumour should be undertaken without the accurate localization of the tumour by the usual methods of clinical differentiation and objective demonstration, supplemented, if at all possible, by

cerebral angiography of Moniz, which is the only procedure capable of definitely determining that the tumour is an aneurysm and not neoplasm. The disastrous consequences of mistaking an aneurysm for a neoplasm cannot be overemphasized. It is practically impossible in the vast majority of these aneurysms to obliterate them without interrupting the circulation in the circle and seriously impairing the nutrition of the area of the brain that is supplied by the arteries given off from the circle beyond the obliterated branch. It should be remembered in arriving at conclusions before operation that, though the tendency and fate of an intracranial aneurysm is to end fatally in apoplectic rupture, or after a succession of leaks and limited extravasations (especially in the aged with brittle sclerotic arteries complicated with arterial hypertension), it is quite possible, especially in young subjects with fairly elastic arteries, that spontaneous cure by thrombosis may be effected in some cases, and, in others, the enlargement and rupture of the aneurysm may be indefinitely averted by the calcification and encapsulation of the sac. FRANK TURNBULL

The Ayala Index. Savitsky, N. and Kessler, M., *Arch. Neurol. & Psychiat.*, 1938, **39**: 988.

The Ayala index is a valuable aid in the differential diagnosis of non-expanding and expanding intracranial lesions. In cases of tumour or abscess of the brain the degree in the drop in pressure after the removal of a given amount of spinal fluid differs from that in cases of otitic hydrocephalus or serous meningitis. The index is computed as the product of the final pressure and the amount removed divided by the initial pressure. The test is only of value in cases in which the initial pressure is above 140 mm. of water. As a standard test it is preferable that exactly 10 c.c. of fluid be withdrawn in every case.

Savitsky and Kessler determined the Ayala index in 186 consecutive cases of increased intracranial pressure. They observed that a low index (below 5.5) is in favour of an expanding lesion. The index was found to be of greatest value in the differential diagnosis of abscess of the brain from otitic hydrocephalus. It was also helpful in the detection of expanding intracranial lesions which occasionally coexist with arterial hypertension. FRANK TURNBULL

Therapeutics

The Present Status of the Management of Varicose Veins. Collective Review. McPheeters, H. O.: *Surg., Gyn. & Obst.*, 1938, **76**: 494.

The combination of ligation at the saphenofemoral junction, with injection of some varicosities at the same time or later, has proved the most effective procedure. The author favours sodium morrhuate; sodium ricinoleate and monoleate are giving fine results. Eczemas and ulcers are still being treated conservatively by the majority, whilst others insist on high ligation with the inclusion of all collaterals. Early ligation with excision of all scar tissue of the old recurrent ulcer area and application of a pedicled or full-thickness graft has its advocates. Two to 5 per cent alcoholic solution of gentian violet, with or without a dusting powder, ultraviolet light, and iontophoresis have their individual proponents. The fungus infection associated with moist eczema may be treated by 1 to 10 Burrows' solution or by 5 per cent alcoholic gentian violet, with support for a long time afterwards. Infective thrombophlebitis is still treated conservatively by the majority, although there are the active few who claim good results with early high ligation. Some are advising active treatment of severe varicosities in pregnancy. The fine superficial bursts and spider flares are being treated by 1 per cent morrhuate with extreme elastoplast pressure over gauze for 5 to 6 days. FRANK DORRANCE

Pathology and Experimental Medicine

The Insulin and Zinc Content of Normal and Diabetic Pancreas. Scott, D. A. and Fisher, A. M.: *J. Clin. Investigation*, 1938, **17**: 725.

Fourteen normal and eighteen diabetic pancreases were obtained at autopsy and the insulin and zinc content of each was determined. In the pancreas of diabetics the total amount of insulin found amounted to only one-quarter of that found in the normal. Likewise, the amount of zinc contained in the pancreas of diabetics was only one-half that normally present. There was no marked difference in the concentration of zinc in the livers of diabetics and of non-diabetics. The possibility of a part of the zinc in the pancreas being concerned with the storage of insulin is suggested. JOHN NICHOLLS

The Study of Some of the Physiological Effects of Sulphanilamide. II. Methæmoglobin Formation and its Control. Hartman, A. F., Perley, A. M. and Barnett, H. L.: *J. Clin. Investigation*, 1938, **17**: 699.

The authors studied the factors leading to the accumulation and to the disappearance of methæmoglobin in patients to whom sulphanilamide had been administered. They came to the following conclusions.

A reasonably close agreement exists between the direct spectroscopic determination of methæmoglobin and the determination of non-oxygen-carrying hæmoglobin. In the great majority of patients receiving 0.1 g. or more of sulphanilamide per kg. in 24 hours cyanosis develops, and the authors were able to demonstrate the presence of methæmoglobin in every case of cyanosis.

There is a marked individual variation in both the rate at which and the degree to which methæmoglobin accumulates, although the dosage of sulphanilamide, its concentration in the blood, and perhaps also the extensiveness of the infection, seem to have a direct relationship.

Methylene blue causes a very rapid disappearance of the cyanosis, with simultaneous reduction in methæmoglobin concentration when given intravenously in single dose of 1.0 to 2.0 mg. per kg., or when given orally in doses of 1.0 to 2.0 grains (65 to 130 mg.), repeated every four hours. The latter method also prevents any appreciable formation of methæmoglobin if started simultaneously with the administration of sulphanilamide. JOHN NICHOLLS

Carbohydrate Tolerance after Protamin Insulin: its Bearing on the Physiology of Insulin Secretion. Ricketts, H. T.: *J. Clin. Investigation,* 1938. **17**: 795.

The author found that in severe diabetes, when the fasting blood sugar is brought to normal by protamine insulin, post-prandial hyperglycæmia is not controlled without additional insulin. Under similar conditions the blood sugar curves of mild diabetes approach the normal.

These facts do not support the contention that the liver operates to reduce hyperglycæmia without the aid of extra insulin. They do offer new evidence in favour of certain old theories, namely, (1) that, normally, the ingestion of carbohydrate stimulates the secretion of insulin by the pancreas; (2) that the pancreas of the severe diabetic responds poorly to such a stimulus; (3) that the pancreas of the mild diabetic retains enough of its excretory function to react when so stimulated by secreting an additional, though still not optimum, amount of insulin; (4) that the blood sugar curve of a normal person may be regarded as the result of a completely adequate pancreatic response.

JOHN NICHOLLS

The Use of a Globulin Substance Derived from Beef Plasma as a Local Hæmostatic in Hæmophilia. Pohle, F. J. and Taylor, F. H. L.: *J. Clin. Investigation,* 1938, **17**: 677.

Previous studies indicated that the defect in coagulation of the blood in hæmophilia resides in a plasma globulin fraction. This "globulin substance", when prepared from citrated cell-free beef plasma by isoelectric precipitation at pH 6.0, possesses properties similar to that prepared from normal human plasma except that it has slightly greater clot-accelerating properties for hæmophilic blood *in vitro*. The oral administration of beef "globulin substance" to adult hæmophiliacs is without effect on the coagulation-time of the blood in the doses employed. But when it is applied locally in the form of a dry powder it is an effective hæmostatic in hæmophilia. JOHN NICHOLLS

Hygiene and Public Health

The Relation of Human Encephalitis to Encephalomyelitis in Horses. Elkund, C. M. and Blumstein, A.: *J. Am. M. Ass.,* 1938, **111**: 1734.

During August and September, 1937, six cases of human encephalitis were reported from a county in northwestern Minnesota. All were in farmers. Five had had contact with sick horses. The sixth had had no contact but lived in Dakota not far from the Minnesota border. The blood serum from one of the cases was shown to neutralize the western strain of equine encephalomyelitis. FRANK G. PEDLEY

Human Encephalitis: Eight Fatal Cases with Four Due to the Virus of Equine Encephalomyelitis. Wesselhoeft, C., Smith, E. C. and Branch, C. F.: *J. Am. M. Ass.,* 1938, **111**: 1735.

In August, 1938, an outbreak of equine encephalomyelitis causing the death of more than 200 horses occurred in southeastern Massachusetts and Rhode Island. On August 12th a girl, aged 12, was admitted to the Haynes Memorial Hospital, Boston, with what proved at autopsy to be encephalitis. On August 29 a boy, aged 13, was admitted from the same locality. He also died, presumably from encephalitis, but no autopsy was permitted. Six more patients were admitted to the Haynes Memorial Hospital during September, all of whom died, and 18 others were admitted to other hospitals in Boston. The clinical course of the 8 cases in the Haynes Memorial Hospital is given together with the autopsy findings on 7. In four of these cases the virus of the eastern strain of equine encephalomyelitis was recovered from the brain. The Rockefeller Institute cooperated in this. Present epidemiological and experimental evidence points to the spread of the infection by an insect vector (probably a mosquito) rather than by direct contact. None of the reported cases had come in contact with horses.

FRANK G. PEDLEY

Obituaries

Dr. Leslie Roy Aitken, of Courtright, Ont., died suddenly on November 16, 1938, aged fifty-one. Dr. Aiken was born at Mandaumin and received his early education there and at the Sarnia Collegiate Institute. He later attended London Normal School and qualified as a teacher. He taught at Wilkesport and S.S. No. 1 Sarnia Township and then gave up teaching to take a medical course at the University of Western Ontario. In 1913 he graduated from the university and shortly afterward commenced practising in Courtright, where he continued for the 25 years up to his death. He developed a large practice which required a branch office at Corunna. He was also a coroner.

Dr. William H. Kalbfleisch, mayor of Balgonie, and one of the best-known pioneer physicians of central south Saskatchewan, died on November 15,

1938, aged seventy. He was born in the United States shortly before his father and mother went to Herrington, Oxford County, Ontario. Following his graduation in medicine from the University of Western Ontario in 1898 he came west and settled at Balgonie more than 35 years ago. He had been mayor of the town for many years, and also operated a drug store. He retired from active practice two years ago. He was unmarried.

Dr. John Archibald MacMurchy, of Dresden, Ont., died on November 28, 1938, in his fifty-fourth year. He was a graduate of the University of Toronto (1916).

Dr. Samuel Alexander McKeague, of Winnipeg, died on December 9, 1938, aged eighty years. He was born at Wellandport, Ont., and graduated from Trinity University, Toronto, in 1884. He had been in active practice in Winnipeg from 1904 until his retirement in 1928.

Dr. Angus A. McLean, of Mount Forest, Ont., died on November 9, 1938. He was the youngest son of the late Dugald and Mrs. Nancy (Munroe) McLean, and was born in 1879, in Clachan, Elgin County. After attending Clachan public school and Ridgetown High School he enrolled in Chatham Model School and for three years taught school in Tilbury. He entered Toronto University, and following graduation in 1907 he took over the practice of Dr. Peter Pavey, at Duart, Ont., remaining there for 10 years. In 1917 he began practice in London, and then took post-graduate work in St. Luke's Hospital, Chicago. He returned to his practice in London, and, more recently, in Mount Forest. He was coroner of the Mount Forest district.

Dr. Robert Alvin McLurg, aged 61, of Wilkie, Sask., died on November 5, 1938. He was born at Petrolia, Ont., was educated at Woodstock, and graduated from Trinity Medical College, Toronto, in 1904, as his father and two uncles had done before him. He was a nephew of Dr. John McLurg, Bay City, Michigan and Dr. David McLurg, Detroit. He did post-graduate work at the New York Post-graduate Hospital, at the Mayo Clinic, and at Chicago. He first practised at Helen Mine, Michipocoton, and later at Battleford, where he established a railway hospital. He came to Wilkie in 1908. During his residence at Wilkie he was Canadian Pacific Railway doctor.

He worked untiringly and unceasingly in the best interests of the community. Times without number he faced storms and blizzards, using every kind of method of transportation at any hour of the day or night, regardless of weather and severe personal discomfort; in days past, without benefit of highway, municipal roads, fences, telephone lines, or other guiding aids he broke trail in the darkness to many a farm home. During the influenza epidemic he commandeered essential services and established an emergency hospital in the Wilkie School where hundreds of patients were looked after, with no deaths.

For the past fifteen years he was a member of the Wilkie School Trustee Board. Through his efforts the Wilkie Mechanics Institute Library came into existence. He was a member of the Wilkie Board of Trade. He was instrumental in organizing the local Boy Scouts and was active in the Red Cross. He was past president of the Saskatchewan Medical Association.

In grateful acknowledgment of Dr. McLurg's service to his community a bronze tablet is being placed in the Wilkie School, which is henceforth to be known as the McLurg School.

Dr. George Brown Mills, of Alsack, Sask., died on November 15, 1938, aged seventy. He was a master of surgery and at one time associated with the Mayo Brothers Clinic at Rochester. He was born and received his early education at Fergus, Ont. He graduated from Trinity College, Toronto, in 1896, coming west shortly after; he practised first at Carnduff, Sask. and then several years in Senlac. He came to Alsask a year ago.

Dr. Samuel Jacob Morris, of Mount Elgin, Ont., died on November 5, 1938. Dr. Morris was born in North Dorchester Township, had taught school there, and in 1900 graduated from Western University, London, immediately afterwards taking up practice of his profession in Mount Elgin. He practised there continuously for 30 years. He retired eight years ago.

Dr. Ernest Evelyn Sinclair, of Summerside, P.E.I., died on November 20, 1938, aged fifty-seven. He was a graduate of McGill University (1905) and St. Bartholomew's, London, England. He first practised in Nova Scotia, later moving to Summerside.

Dr. Robert Telford, of Vancouver, died on November 10, 1938. He was born in Ontario in 1869 and came to British Columbia many years ago, teaching school on Vancouver Island for a short time. Then he entered McGill University where he graduated from the medical college (1898). Returning to British Columbia he practised in Nanaimo and Chemainus before settling in Vancouver.

Dr. John Henry George Youell, of Aylmer, Ont., died on November 28, 1938, in his seventy-seventh year. He was a graduate of the University of Toronto (1892).

News Items

Alberta

The Council of the College of Physicians and Surgeons is holding elections in the following districts, Lethbridge, Camrose and Calgary, but as only one accepted nomination in Camrose and Calgary, Dr. W. V. Lamb and Dr. R. B. Francis were elected to succeed themselves. Three candidates are running in the Lethbridge district, Drs. A. A. Haig, J. K. Mulloy and S. M. Schmaltz. Ballots will be counted December 31, 1938.

According to the new Workmen's Compensation Act, injured workmen are permitted to go to chiropractors for treatment, but, by arrangement with the Chiropractic Association members of that cult agreed with the Chairman of the Workmen's Compensation Board to send injured workmen to registered medical practitioners who were to examine them and return them to the chiropractor if such treatment were indicated. No decision of the medical practitioner in any way limited the injured workman in his choice of chiropractic treatment. Very few cases are reported as receiving chiropractic treatment.

Last year the physicians had special auto plates as follows: Med. 293 followed by a green cross. In some cases medical men felt this distinguishing mark made their cars open to thieves, and uttered their protests to the Press which "played it up" reflecting on the Government. This was unfair as the Government had acted only at the request of the profession in issuing the special number plates. No special plates have been ordered, but arrangements are under way to reserve to the members of the profession a special series of numbers.

The College of Physicians and Surgeons are in communication with the Government in an endeavour

to have a Cancer Remedy Act similar to that of Ontario passed in Alberta. There is a strange anomaly here, inasmuch, as cancer is a reportable disease here, as far as the medical profession is concerned, but, irregulars claim to be treating cancer and are not compelled to report their cases.

Recently the Workmen's Compensation Board adopted a new form of accident report and sent supplies to the employers. When an accident occurred the injured workman was supposed to present the form, completed as far as he himself and his employer were concerned, to the physician, so when the latter filled in his portion, the report was complete and there would be no delay and no confusion of names. In carrying out this new system the weak part was that too frequently the injured workmen rushed to the doctor first, and if the case was not one for compensation, he got his treatment but did not produce the form or report the accident to the employer. Now, if the workman does not produce the form the physician uses the old form to report direct to the Board.

According to the new highway regulation the bus and truck drivers must produce a certificate from a physician showing that their health is in good condition and their eyesight and hearing are not impaired to the danger of road traffic. The forms indicated that the examination must be most thorough.

At a recent meeting of the Council of the College of Physicians and Surgeons a resolution of appreciation of the services of Dr. W. S. Galbraith to the profession and also to the public was passed unanimously.

At a special meeting of the Calgary Medical Society held on December 6, 1938, Sir Frederick G. Banting, representing the Associated Committee of Medical Research of the National Research Council of Canada, addressed a largely attended meeting on cancer research. The speaker traced the development of investigations into the causes of cancer from late in the nineteenth century to the present time. He outlined some of the experimental work which has been done in recent years in cancer research. His address was greatly appreciated by the members of our Society.

The annual conjoint meeting of the Alberta Hospital Association and the Alberta Municipal Hospitals Association was held on November 28 and 29, 1938, at the Palliser Hotel, Calgary. Various problems in connection with hospital management and nursing were discussed. Among these were the questions of visitors to hospitals, medical interns, the medical staff, fire regulations and drill, dietetians, radios, the hospital pharmacy, hospitals and isolation, convalescent homes, auditors, numerous questions pertaining to the nursing profession, local improvement districts, municipal districts and indigents. Dr. Harvey G. Agnew, Secretary of the Department of Hospital Services, Canadian Medical Association, gave an address on "What is new in the hospital field".

G. E. LEARMONTH

British Columbia

On November 7th His Honour Lieut.-Governor E. W. Hamber officiated at the opening of the new x-ray department of St. Joseph's Hospital, Victoria.

St. Joseph's Hospital has recently replaced its x-ray equipment with new, the major part of which was made in Canada by the Ferranti Electric Company, of Toronto. This new apparatus includes a 400,000 volt x-ray therapy equipment and is the fifth supravoltage installation in Canada. There is also a three-phase transformer for diagnostic work, which is the first of its kind in Canada. The equipment includes numerous modern improvements, making the department one of the most thoroughly equipped in Canada. The installation will be under the care of Dr. Andrew Turnbull, a graduate of the University of Manitoba Medical School. Dr. Turnbull did general practice in Athabasca, Alta., for four years and spent three years on a Fellowship in radiology at the Mayo Clinic. He is a Diplomate of the American College of Radiology and practised radiology in Durham, N.C., prior to coming to Victoria.

On November 5, 1938, the first unit of the British Columbia Cancer Foundation was opened in the former interns' home on the grounds of the Vancouver General Hospital by Lieut.-Governor E. W. Hamber. Dr. A. Maxwell Evans has been appointed as permanent radium therapist.

Sir Frederick Banting has been visiting Vancouver as Chairman of the Special Committee set up by the National Research Council. He was here to examine facilities for medical research across Canada and has had a busy time inspecting the General Hospital, the Cancer Institute, and laboratories of the Provincial Board of Health. He spoke, also, to premedical students at the University of British Columbia. Sir Frederick was accompanied by Dr. C. B. Stewart, Assistant Secretary, Associate Committee on Medical Research.

The corresponding members of the Committee on Economics of the Canadian Medical Association, whose Chairman is Dr. Wallace Wilson, of Vancouver, are as follows: Drs. R. Vance Ward, Montreal; A. F. VanWart, Fredericton; H. B. Atlee, Halifax; E. S. Moorhead, Winnipeg; D. P. Miller, Prince Albert; H. C. Wales, Toronto; S. M. Rose, Lethbridge; R. F. Seaman, Charlottetown; W. A. Clarke, New Westminster. This Committee is considering several important problems during the coming year, notably questions of contracts and the all important subject of health insurance from a national point of view.

Dr. D. J. Bell, of Vancouver, recently celebrated his fiftieth year as a medical practitioner in active practice, and was honoured by a dinner and presentation given by his patients and friends in the part of Vancouver where he lives and practises.

Another medical man shares similar experience with that of Dr. Bell, namely, Dr. W. A. Richardson, of Campbell River, Vancouver Island, who has also practised in British Columbia for fifty years, having graduated in 1886 from Toronto University. Like Dr. Bell, he is still in practice, and his colleagues and friends of the Upper Vancouver Island area gave him a dinner and made him a presentation in recognition of his long and devoted services.

J. H. MACDERMOT

Manitoba

Manitoba was privileged to receive a visit from Sir Frederick Banting on November 28th and 29th. On the former date he addressed the students of the Faculty of Medicine on "The value of research", and on the following day he was the principal speaker at a luncheon in his honour, under the auspices of the Winnipeg Medical Society, at the Fort Garry Hotel. On this occasion Sir Frederick referred to the research work being carried on in the Banting Institute in Toronto, and stressed the value of cooperation in research.

Dr. Harvey Agnew, Associate Secretary of the Canadian Medical Association, was a welcome visitor in Winnipeg on November 24th.

ROSS MITCHELL

New Brunswick

During his visit to the Maritimes Sir Frederick Banting visited universities and hospitals in New Brunswick, and renewed many friendships, especially with war-time comrades. While in Saint John he was entertained by His Honour, Lieut.-Governor Dr. Murray

MacLaren and by the Byng Boys Club. During his visit to the Provincial Hospital at Fairville, N.B. he was much interested in the use of insulin shock in the treatment of schizophrenia. This work has been done under the direct supervision of Dr. W. O. McDonald. Sir Frederick was the guest speaker at a complimentary luncheon at which His Honour the Lieut.-Governor was the host to the Saint John Medical Society.

Dr. E. A. Petrie was the special speaker at the last monthly meeting of the Saint John Medical Society. Dr. Petrie's subject was "Refinements in diagnosis in chest lesions", particularly the diagnosis of these lesions by x-ray. The subject is of most active interest to clinicians, and the discussion was brisk both from the x-ray and clinical sides.

Lieut.-Col. R. A. Hughes has just returned from Ottawa where he attended the meeting of Defence Medical Council.

Dr. J. A. M. Bell, who has practised in Newcastle for many years, has moved to Fredericton.

Drs. A. L. Donovan and J. R. Nugent have just returned from post-graduate work at the Lahey Clinic, Dr. Nugent following the surgical treatment of gastro-intestinal and bowel lesions, while Dr. Donovan attended the Cardiac Clinic at the Lahey Clinic and the Peter Bent Brigham Hospital.

The Council of Physicians and Surgeons of New Brunswick at their fall meeting passed a resolution stating that in future enabling certificates for candidates wishing to take the examination of the Dominion Medical Council will be only issued to Canadian students.

At the November meeting of the Executive Committee of the New Brunswick Medical Society further steps were taken to complete arrangements for federation with the Canadian Medical Association. Notice of motion was given for a change in the constitution providing that the New Brunswick member of the Canadian Medical Association Executive should be *ex-officio* a member of the Executive Committee of the New Brunswick Society.

A late November blizzard caused much difficulty and unpleasantness to all rural practitioners in New Brunswick, due to blocking of the roads and destruction of telephone and telegraph communications. This storm also trapped Dr. H. A. Farris, of Saint John, in his hunting camp twenty-seven miles from Chipman, from which he was extricated with considerable difficulty.

Dr. R. M. Pendrigh has been granted his majority in the Royal Canadian Army Medical Corps.

A. S. KIRKLAND

Nova Scotia

The Canadian Society for the Control of Cancer held its first, local, public meeting at Halifax recently, with Dr. Alexander Primrose as the guest speaker. The proposal that a small fee be levied on members to make possible the distribution of literature on cancer was favourably received.

Dr. A. S. Cowie (Dal. '33), has taken up medical practice in Wolfville. For the past three years Dr. Cowie has been located at Salisbury, N.B.

Dr. G. H. Murphy was elected president of the St. Francis Xavier University Club of Halifax at its annual meeting.

That the Yarmouth Gateway Hospital has achieved a rare fame was shown at the annual meeting when the president reported an operating surplus for the year of $106.47.

Dr. Frank E. Walsh was elected vice-president of the Cumberland Branch of the Canadian Tuberculosis Association at a recent meeting at Amherst.

According to the reports of the Royal Canadian Mounted Police there are "very few" dope addicts in Nova Scotia, Halifax being completely free of them. It is hoped that locally, as in British Columbia, legislation may soon be enacted to prevent the sale of codeine without a prescription.

Dr. Harold Taylor (Dal. '36), is leaving Port Morien, where he has been associated with Dr. W. W. Patton, to take up the study of pathology at Edinburgh.

ARTHUR L. MURPHY

Ontario

On December 7th Prof. William Boyd, of the University of Toronto, delivered the Thomas Dent Mütter Lecture at the College of Physicians of Philadelphia, on the subject, "Some reasons for the recent increase in bronchial carcinoma".

Tribute was paid to Drs. W. W. Moffatt and S. V. Railton, of Welland, who were recently successful in the examination for the degree of Fellow of the Royal College of Physicians and Surgeons of Canada. Some sixty guests assembled at dinner to express the esteem and admiration in which these doctors were held by their colleagues in the Niagara peninsula, by laymen active in hospital work and municipal affairs, and by representatives of the County Medical Societies of the district.

Dr. Robert Charles Norman, of Toronto, has been admitted to Fellowship in the Royal College of Surgeons of England.

The Academy of Medicine, Toronto, is holding its annual Library and Historical Night on January 3, 1939. One of the features of this meeting will be the display of that portion of the library which friends of the late Dr. Oskar Klotz have presented to the Academy, dealing with the History of Pathology.

The Sisters of St. Joseph announce that they will begin work on the new Hospital for Incurables to replace the present Mercy Hospital on Sackville Street. It will be erected on Sunnyside Avenue near St. Joseph's Hospital. Two hundred and fifty beds are planned. The vacated beds of Mercy Hospital will be made available to the House of Providence.

The County of Renfrew is obtaining estimates for the cost of construction of a County Sanatorium.

The Ontario Hospital financial year ends on September 30th. Many of our hospitals have already held their annual meetings. Some of the impressions of the local press may be worth recording.

The St. Lawrence Sanatorium has completed its first year with 167 patients. The financial affairs of the Sanatorium seem to have been satisfactory.

The Niagara Peninsula Sanatorium reports all beds filled throughout the year. An extra physician has been added and also a laboratory technician. All laboratory work has increased during the year. The work done by the patients was exhibited at the Canadian National Exhibition, taking thirteen prizes with twenty-one entries. One hundred and seventy-

three patients were treated, with an average of 80 patients in residence.

The Freeport Sanatorium has re-elected its directorate and appears to have balanced its budget. Average number of patients in residence, 133.

The Brant Sanatorium reports 87 patients in residence at the close of the year. The services have been enlarged. Many necessary renovations have been made and modern laundry equipment has been installed.

All the sanatoria appear pleased with the new regulations whereby the province assumes the cost of medical care of the indigent patient.

From the hospital reports available we glean that the hospital at Barrie has made many important improvements costing $13,500. One thousand one hundred and ninety-six patients were admitted. The mortgage debt has been wiped out and a new elevator installed.

St. Andrew's Hospital, Midland, has a small operating profit, fewer patients, and a slightly longer average stay. A new central heating plant has been installed and a new wing is nearing completion.

At the Great War Memorial Hospital, Perth, the Danner Memorial Pavilion is nearing completion. Nine hundred and sixteen patients were admitted. There is a small net surplus for the year.

The Port Arthur General Hospital reports the best year in its history. The Nurses' Home is now nearing completion. The Hospital has been crowded. Average number of patients per day, 73.5. New x-ray equipment has been installed.

The Port Hope Hospital reports a deficit of nearly $4,000, despite higher revenue.

The Pembroke Cottage Hospital shows an increase of over $5,000 in expenses, also an increase in the number of patients and in hospital fees collected. The operating deficit for the year was $1,271.00. The institution is now staffed with graduate nurses.

The Welland County General Hospital had an average of 50 patients in residence. Considerable new equipment has been added.

The Norfolk General Hospital at Simcoe established two records—1,498 patients were treated during the year, and there were 276 births at the hospital.

The Metropolitan Hospital at Windsor expects a deficit of $36,000. There has been a large increase in the number of indigent patients treated during the year.

The Memorial Hospital, St. Thomas, announces that alterations are being made in the Children's Shelter Building, to provide a new residence for nurses. The space occupied by the nurses in the old hospital will be used for additional beds for patients. The hospital has been overcrowded.

The Toronto Hospital for Incurables reported better accommodation and treatment for the largest number of patients in its 64 years of operation. The financial statement revealed a small deficit of some $8,500 as against operating expenses of $275,000 for the year.

The Red Cross Hospital at Richards Landing reports a successful year with a small balance in hand.

The Clinton Community Hospital presented encouraging reports. Its finances are in excellent shape and its equipment has been materially improved.

The Prince Edward County Hospital at Picton shows a small operating balance. Seven hundred and forty-two patients were treated. About 22 per cent of the total operating revenue was received from municipalities for indigent patients.

The Soldiers Memorial Hospital at Orillia showed a small net surplus on the year's operations. Daily average of patients, 56; babies born, 226. The debenture debt is being taken care of.

The Ingersoll Hospital reported that last year was the biggest year of the hospital with an operating loss. Heavy expenditures were necessary for improvements and replacements.

The Paris Willett Hospital records the completion of new buildings with modern equipment. The payment of $54,000 is to be spread over two years. More patients were cared for than ever before.

The Douglas Memorial Hospital, Fort Erie, reports an increase of 73 patients over the previous year.

The Plummer Memorial Public Hospital at Sault Ste. Marie has completed the most successful year in its history. Admissions were 264 above the year 1937, while births were increased by 49.

The Public General Hospital at Chatham reported the payment of over $30,000 toward the construction of the new $100,000 wing. The new wing will be ready for occupation about February 1st. The operating loss of about $7,000 is more than last year.

The Galt Hospital reports a deficit of over $11,000 on the year's operations. The number of hospital days for free patients showed a large increase.

The Cornwall General Hospital admitted 719 patients and treated 748 out-patients. The operating room was enlarged and improved. Average days' stay, 13.05; average number of patients in residence, 61.3. Thirty-five nurses are in training.

The Alexandra Marine and General Hospital at Goderich has a small operating balance for the year. Average days' stay per patient, 14.16. Total number of patients treated, 647.

J. H. ELLIOTT

United States

The American Board of Ophthalmology announces an important change in its method of examination of candidates for the Board's certificate.

Examinations will be divided into two parts. Candidates whose applications are accepted will be required to pass a written examination which will be held simultaneously in various cities throughout the country approximately 60 days prior to the date of the oral examination. The written examination will include all of the subjects previously covered by the practical and oral examinations.

Oral examinations will be held at the time and place of the meeting of the American Medical Association and of the American Academy of Ophthalmology and Oto-Laryngology, and, occasionally, in connection with other important medical meetings. The oral examination will be on the following subjects: External Diseases, Ophthalmoscopy, Pathology, Refraction, Ocular Motility, Practical Surgery. Only those candidates who pass the written examination and who have presented satisfactory case reports will be permitted to appear for the oral examination.

Examination scheduled for 1939: written, March 15th and August 5th. Oral: St. Louis, May 15th; Chicago, October 6th. Applications for permission to take the written examination March 15th must be filed with the Secretary not later than February 15th. Application forms and detailed information should be secured at once from Dr. John Green, Secretary, 6830 Waterman Ave., St. Louis, Mo., U.S.A.

The American College of Physicians.—The Twenty-third Annual Session of the American College of Physicians will be held in New Orleans, with general headquarters at the Municipal Auditorium, March 27 to 31, 1939.

Dr. William J. Kerr, of San Francisco, is President and will have charge of the program of general scientific sessions. Dr. John H. Musser, of New Orleans, has been appointed General Chairman of the Session, and will be in charge of the program of clinics and demonstrations in hospitals and medical schools and of the program of round-table discussions to be conducted at the headquarters. The Executive Secretary is Dr. E. R. Loveland, 4200 Pine St., Philadelphia, Pa.

Book Reviews

The Living Body. C. H. Best, M.A., M.D., D.Sc., F.R.S., F.R.C.P.(C.), and N. B. Taylor, M.D., F.R.S.(C.), F.R.C.S., F.R.C.P.(C.), M.R.C.S., L.R.C.P. 563 pp., illust. $3.60. Henry Holt & Co., New York, 1938.

This book has been written for the sole purpose of providing a text for students in college, or comparable groups, who desire to learn of the functions of the human body. It would seem that the authors have been unusually successful in the organization and presentation of their subject. A nice balance has been maintained as regards the allotment of space to the various subjects. The book is essentially readable and readily understandable. It will be particularly welcomed by teachers giving courses to college students, nurses and others for whom a reliable, comprehensive and clear text is desired. It is to members of the medical profession who are responsible for this type of teaching that this book is unreservedly recommended.

Textbook of Nutrition. J. A. Nixon and D. G. C. Nixon. 219 pp., illust. $2.50. McAinsh, Toronto, 1938.

This textbook can be unqualifiedly recommended to all physicians who are interested in nutrition. It is excellently written and contains a wealth of information not only on the fundamental principles of nutrition but on food values and the practical application of this knowledge in the everyday work of the physician.

The book expresses the views held by many of the conservative medical men and investigators interested in nutrition in Great Britain. There are some points of minor importance with which the reviewer does not agree. For instance, on page 56 it is stated, "Vitamin D is only found in a limited range of foods, of which the chief are fish-liver, egg yolk, milk, butter, and fresh green leaves. Milk shows a seasonal variation according to the cow's feed." From this the reader might infer that if he included egg yolk, milk, butter and green leaves in the diet he might be supplying an adequate amount of vitamin D. Canadian green leaves do not contain vitamin D in appreciable amounts, as it has been found to take some thousands of servings of green leaf food, such as spinach, to furnish the vitamin D equivalent of 1 teaspoon of cod liver oil. It is obvious that milk is not a source of vitamin D as rickets develops in infants whose sole food intake is milk. Although the book was published in 1938, no mention is made of nicotinic acid.

On page 163 is the statement, "The practice of giving cereals and cereal products to young infants cannot be too strongly condemned." This statement of course is not in accord with the universal practice in Canada of adding cereal products to the diet of young infants. The reviewer has quite an open mind on the subject, but feels that this statement is a rather strong one to make without giving evidence in detail in support of it, particularly as this view is contrary to the belief of most pædiatricians and nutritionists. The above adverse criticisms of course are of a very minor nature. The authors are to be congratulated on producing this most interestingly written and valuable book.

Anus, Rectum and Sigmoid Colon. Diagnosis and Treatment. Harry Ellicott Bacon. 804 pp., illust. J. B. Lippincott, Company, Philadelphia, 1938.

This volume covers the field of the anus, rectum, and sigmoid in a most thorough and painstaking manner. Dr. Bacon is associated with the department of proctology at the Graduate School of Medicine of the University of Pennsylvania and not only does he include the practice of this school in dealing with lesions of the terminal bowel but he also includes the accepted methods of other workers. The book is almost encyclopædic in scope. The illustrations are beautifully done, and there are important chapters on such subjects as lymphogranuloma inguinale, chancroid, wounds and injuries, and tuberculosis.

This work must at once appeal both to general surgeons and to men particularly interested in lesions of the lower bowel.

Clinical Roentgenology of the Digestive Tract. M. Feldman, M.D. 1014 pages, illust. $10.00. Wm. Wood, Baltimore, 1938.

This book is an excellent contribution to the study of the gastro-intestinal tract. It is a valuable compilation of data with coordination of clinical and radiological facts in reference to the entire tract but mostly of value in reference to the stomach. The illustrations are plentiful with concise explanatory notes. Not only as a textbook but as a quick, ready and complete reference, "Clinical Roentgenology of the Digestive Tract" is an asset to the general practitioner and the radiologist.

The Primate Thalamus. A. E. Walker, M.D. 322 pp., illust. $3.00. University of Chicago Press, 1938.

The scope of this valuable monograph is indicated not so much by the title, which may suggest a limited survey of only indirect value to medicine, but rather by the author's concluding sentences: "It [the thalamus] is the mediator to which all stimuli from the outside world congregate and become modified and distributed to subcortical or cortical centres so that the individual may make adequate adjustments to the constantly changing environment. The thalamus thus holds the secret of much that goes on within the cerebral cortex".

Dr. Walker, who is an Instructor in Neurosurgery in the University of Chicago, has conducted experimental research on the thalamus in three American universities and in the Laboratory of Neuropathology at Amsterdam, choosing to work on the macaque monkey because its thalamus resembles in many important respects that of man. In this book he correlates his results with those of other experimenters, with anatomical, physiological, pathological and clinical findings, in a wide survey with a comprehensive bibliography extending from the time of Galen to the present year. The numerous details are so treated as not to obscure the main issues, and the volume should prove very useful, not only to anatomists, physiologists, pathologists and neurologists but to any physician who wishes to be up to date in his understanding of disorders of sensation.

Endocrine Therapy in General Practice. E. L. Sevringhaus, M.D., F.A.C.P. 192 pp. $2.75. Year Book Publishers, Chicago, 1938.

To the general practitioner this volume should prove of great value. The author briefly, but clearly discusses the biological significance of the hormones; treats each gland of internal secretion under a separate heading, stressing the function of the gland, the pathology of hypo- or hyperfunction and therapy of the disease in question. The chapter on obesity is exceedingly instructive. The book is well and helpfully illustrated.

Laboratory Manual of Hæmatologic Technique. R. C. Beck, M.A., M.D. 389 pp., illust. $4.50. Saunders, Phila., 1938.

This is a most comprehensive laboratory book of hæmatological technique for the laboratory workers. It is clearly written, well illustrated, and with summaries and list of questions at the end of each chapter to aid the student in self-quizzing. The chapters related to the study of bone marrow and vital staining are especially well presented. The book should be very useful to students and technologists.

Classified Advertisements

WANTED.—Municipal doctor, Government grant approximately $250.00 per month available with possible added remuneration from villages. Applicants state age, qualifications, salary expected. Secretary-Treasurer, Rural Municipality, Excel No. 71, Viceroy, Sask.

WANTED.—Three positions as permanent assistants in a Hospital Clinic will be available shortly. We would prefer young men, under 30, with special training in: First, Pædiatrics, secondly, Orthopædics and Surgery; thirdly, Internal Medicine. State all qualifications and send photo in first letter. Apply Box 314, Canadian Medical Association Journal, 3640 University Street, Montreal.

INTERNSHIP WANTED.—Married L.M.C.C., B.A., M.D., C.M., McGill, D.T.M. & H., London, 2 years' internship, age 30, would like assistantship in general or surgical practice with view to partnership or future purchase. Extensive tropical, surgical and pathological experience. Apply Box 313, Canadian Medical Association Journal, 3640 University Street, Montreal.

TO RENT.—Doctor's office and residence. Just vacated, in village in new rich tobacco county (Norfolk). This year's crop income, fourteen million dollars. No resident opposition. Exceptional opportunity. Low rental. R. Mason, General P.O., 231, Toronto.

Principles and Practice of Perimetry. L. C. Peter. 4th ed., 331 pp., illust. $4.50. Lea & Febiger, Phila., 1938.

This edition, like the previous ones is based on a course of lectures on perimetry given by the author in the Post-graduate School of the University of Pennsylvania. Substantially the book remains the same. Some changes, however, have been made in the anatomical and physiological interpretation of studies on the field. New field examples and some charts have been added. These have been designed to clarify the presentation of the material. The only criticism that one could make of this book is that the author tends to be too dogmatic. Dogmatism is often justifiable in a course of lectures but in a textbook tends to narrowness of outlook. For instance, in speaking of idiopathic night-blindness, the author states that "the choroidal circulation is at fault, and the retinal anæsthesia and loss of adaptation are the result of an altered blood-supply to the neuro-epithelial layer of this structure". Recent work has cast doubt on this theory, and it should not be stated so dogmatically. The same criticism can be leveled at the statement that "Migraine is a neurosis." Except for this fault, the book is an excellent piece of work and a worthy addition to the library of the student of ophthalmology.

Statistical Tables for Biological, Agricultural and Medical Research. R. A. Fisher and F. Yates. 90 pp. 12s. 6d. Oliver and Boyd, Edinburgh, 1938.

The use of statistical methods in every branch of medical research is continually increasing, and in most of the branches the only adequate methods are those developed by, or under the direction or inspiration of, Professor R. A. Fisher. The present volume is much more than a reprint of the tables in Prof. Fisher's well known "Statistical Methods for Research Workers". Those tables are reprinted here, some of them in expanded form, but many other tables are also given for use in conjunction with his methods—tables that are not accessible elsewhere. There can be no doubt that this book will soon be considered indispensable to those who use the senior author's "Statistical Methods" or Mainland's "Treatment of Clinical and Laboratory Data", recently reviewed in these columns.

Even workers who do not use statistical methods will find here, in a form very convenient to handle, an economical collection of tables, legible and on sturdy paper—five-figure common logarithms (occupying only two pages), five-figure natural logarithms, square roots of numbers up to 10,000, factorials of numbers up to 300, reciprocals, mathematical and physical constants, mechanical and electrical units, atomic weights, densities, saturated vapour pressures, and the various systems of weights and measures.

Internships and Residencies in New York City, 1934-1937, Their Place in Medical Education. Report by The New York Committee on the Study of Hospital Internships and Residencies. 492 pp. $2.50. Commonwealth Fund, New York, 1938.

The education of the intern and resident can no longer be left to the haphazard arrangements of the hospital and its staff. With the almost unanimous decision of members of graduating classes of today to take increasingly long internships, and with the present-day emphasis upon adequate graduate education as a necessary qualification for specialty recognition, the proper organization of internships upon an educational basis has become accepted as a necessary development to meet modern education needs. Therefore it would seem but natural that the hospitals of New York City, long a Mecca for graduate students, should take stock of their facilities and make recommendations for their improvement.

The five medical schools of New York City and the New York Academy of Medicine, aided by a Commonwealth Fund grant, set up a study committee of leading medical educators under the chairmanship of Frank L. Babbott, with J. A. Curran as Executive Secretary. This report is the result of four years of labour. The resources for intern education are analyzed; the methods of appointment, the schedules adopted, the education during internship, the hospital libraries—all are reviewed. There is a chapter on health care, housing, stipends and intern organizations. One of many conclusions drawn is that the trend towards inclusion of every service in the rotating internship leaves the intern as master of none. "Intelligent selective grouping of the many possible fields of experience available in the modern hospital" is recommended. The urgent need for still better supervision of internships is emphasized, as is also the education of record committees on their responsibilities. Internships should be better integrated with the undergraduate courses. A particularly valuable feature is Appendix Five, which lists the various conditions and procedures which should be covered during the intern course. While the work applies only to New York City, it has a direct application to conditions here, where similar problems are being faced and where it is of value to know the conclusions drawn by this Committee in its exhaustive study.

BOOKS RECEIVED

Psyche and the Physiologists. E. G. Dru Drury, M.D., B.S. 98 pp. 5s. H. K. Lewis, London, 1938.

A History of Women in Medicine. Kate C. H. Mead, M.D. 569 pp., illust. $6.00. Haddam Press, Haddam, Conn., 1938.

Manual of Veterinary Bacteriology. R. A. Kelser, D.V.M., A.M., Ph.D. 3rd ed., 640 pp., illust. $6.00. Williams & Wilkins, Baltimore, 1938.

Alcohol and Human Life. C. C. Weeks, M.R.C.S., L.R.C.P. 2nd ed., 454 pp., 6s. H. K. Lewis, London, 1938.

Minor Medical Operations. K. Harris and E. Harris. 198 pp., illust. 7s. 6d. H. K. Lewis, London, 1938.

Chemical Analysis for Medical Students. R. E. Illingworth, Ph.D., B.Sc. 152 pp. $1.50. Macmillan, Toronto, 1938.

Yearbook of Physical Therapy. Edited by R. Kovács, M.D. 486 pp. $2.50. Year Book Publishers, Chicago, 1938.

Babies are Human Beings. C. A. Aldrich and M. M. Aldrich. 128 pp. $1.75. Macmillan, Toronto, 1938.

The New-born Infant. E. L. Stone, M.D. 2nd ed., 291 pp. $3.00. Lea & Febiger, Phila., 1938.

The Functions of Human Voluntary Muscles. N. D. Royle, Ch.M., F.R.A.C.S. 42 pp. 3s. 6d. Angus & Robertson, Sydney, Australia, 1938.

Biography of the Unborn. M. S. Gilbert. 132 pp. $1.75. Williams & Wilkins, Baltimore, 1938.

How to Conquer Constipation. J. F. Montague, M.D. 244 pp. $1.75. J. B. Lippincott, Montreal, 1938.

Aids to Forensic Pharmacy. A. W. Lupton, M.D., Ph.C., M.P.S. 2nd ed., 260 pp. $1.20. Macmillan, Toronto, 1938.

Our Common Ailment. H. Aaron, M.D. 192 pp. $1.50 Dodge Publishing Co., New York, 1938.